Winter June 15, 2017

A review of Acalypha indicaL. (Euphorbiaceae) as traditional medicinalplant and its therapeutic potential

Nor Syahiran Zahidin, *University Technology Malaysia*
Razauden Mohamed Zulkifli, *University Technology Malaysia*
Ida Idayu Muhamad, *Universiti Teknologi Malaysia*
Harisun Ya'akob, *University Technology Malaysia*
Hadi Nur, *University Technology Malaysia*

Journal of Ethnopharmacology 207 (2017) 146–173

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep

Review

A review of *Acalypha indica* L. (Euphorbiaceae) as traditional medicinal plant and its therapeutic potential

Nor Syahiran Zahidin[a], Syafiqah Saidin[a], Razauden Mohamed Zulkifli[a], Ida Idayu Muhamad[b], Harisun Ya'akob[b,c], Hadi Nur[d,e,*]

[a] *Faculty of Biosciences & Medical Engineering, Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia*
[b] *Faculty of Chemical Engineering, Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia*
[c] *Institute of Bioproduct Development (IBD), Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia*
[d] *Centre of Sustainable Nanomaterials, Ibnu Sina Institute for Scientific and Industrial Studies, Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia*
[e] *Central Laboratory of Minerals and Advanced Materials, Faculty of Mathematics and Natural Science, State University of Malang, Malang 65145, Indonesia*

ARTICLE INFO

Keywords:
Reviews
Ethnopharmacology
Primary healthcare
Traditional medicine Asia and Oceania
Conventional treatment
Acalypha indica L.

ABSTRACT

Ethnopharmacological relevance: *Acalypha indica* is an herbal plant that grows in wet, temperate and tropical region, primarily along the earth's equator line. This plant is considered by most people as a weed and can easily be found in these regions. Although this plant is a weed, *Acalypha indica* has been acknowledged by local people as a useful source of medicine for several therapeutic treatments. They consume parts of the plant for many therapeutics purposes such as anthelmintic, anti-ulcer, bronchitis, asthma, wound healing, anti-bacterial and other applications. As this review was being conducted, most of the reports related to ethnomedicinal practices were from Asian and African regions.

The aim of the review: The aim of this review is to summarize the current studies on ethnomedicinal practices, phytochemistry, pharmacological studies and a potential study of *Acalypha indica* in different locations around the world. This review updates related information regarding the potential therapeutic treatments and also discusses the toxicity issue of *Acalypha indica*.

Materials and methods: This review was performed through a systematic search related to *Acalypha indica* including the ethnomedicinal practices, phytochemistry and pharmacological studies around the world. The data was collected from online journals, magazines, and books, all of which were published in English, Malay and Indonesian. Search engine websites such as Google, Google Scholar, PubMed, Science Direct, Researchgate and other online collections were utilized in this review to obtain information.

Results: The links between ethnomedicinal practices and scientific studies have been discussed with a fair justification. Several pharmacological properties exhibited certain potentials based on the obtained results that came from different related studies. Based on literature studies, *Acalypha indica* has the capability to serve as anthelmintic, anti-inflammation, anti-bacterial, anti-cancer, anti-diabetes, anti-hyperlipidemic, anti-obesity, anti-venom, hepatoprotective, hypoxia, and wound healing medicine. For the traditional practices, the authors also mentioned several benefits of consuming the raw plant and decoction.

Conclusion: This review summarizes the current studies of *Acalypha indica* collected from many regions. This review hopefully will provide a useful and basic knowledge platform for anyone interested in gaining information regarding *Acalypha indica*.

1. Introduction

Before modern drugs began to take shape in the medical care industry, people were highly dependent on natural resources for treatment. This type of treatment, also known as conventional treatment, was the main source of medical treatment during this time (Rao, 1996). However, civilization has changed and with it has come the introduction of more advanced methods, leading the next generations

* Corresponding author at: Centre of Sustainable Nanomaterials, Ibnu Sina Institute for Scientific and Industrial Studies, Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia.
E-mail address: hadi@kimia.fs.utm.my (H. Nur).

http://dx.doi.org/10.1016/j.jep.2017.06.019
Received 19 December 2016; Received in revised form 13 June 2017; Accepted 15 June 2017
Available online 21 June 2017
0378-8741/

Fig. 1. Location of *Acalypha indica*.

to tend to choose modern treatment over conventional treatments. The knowledge and information related to conventional treatments are gradually vanishing since the previous generations are getting older and dying without successors. This knowledge is passed to the next generation, through observation and oral teaching (Nasir, 2012). Therefore, it is crucial to have proper documentation from the extant practitioners since conventional treatments are an alternative path to treat human diseases (Martin, 1995). Conventional or traditional medicinal practices based on natural plants have been recognized by the World Health Organization as reliable medicinal sources for therapeutic activities (WHO, 2002). The medicinal plants are available around settlements, spreading alongside roads, backyards, and house compounds. They can either be collected wild or some people can be found growing them around their house for personal use.

Acalypha indica is a traditional plant, well-known by older generations in many countries, particularly in Asia and Africa. It grows well in most parts of northeast, west, and south of Africa including Ethiopia, Somalia and other regions as shown in Fig. 1 (Aboubaker et al., 2013; Dineshkumar et al., 2010; Discoverlife, 2015; Kankanamalage et al., 2014; Marwah et al., 2007; Masih et al., 2011; NaturalMedicineFacts.info, 2017; Ranju et al., 2011; Schmelzer, 2007; Sivasankari et al., 2014). The plant can also be found in most wet, temperate and tropical countries in Asia, Europe and both South and North American regions. It grows as a weed in backyards, bushes, alongside roads and other places (Chopra et al., 1956; Dineshkumar et al., 2010). Most international manuscripts on *Acalypha indica* were published from Indian region because this plant has a close connection with Ayurveda medicinal practices executed by older Indian generations (Lingaraju et al., 2013; Senthilkumar et al., 2006; Sivasankari et al., 2014).

2. Botanical description

2.1. Taxonomy

There are seventeen synonymous names related to this plant species according to theplantlist.com; these include: *Acalypha bailloniana* Müll. Arg.; *Acalypha canescens* Wall.; *Acalypha caroliniana* Blanco; *Acalypha chinensis* Benth.; *Acalypha ciliata* Wall.; *Acalypha cupamenii* Dragend.; *Acalypha decidua* Forssk.; *Acalypha fimbriata* Baill.; *Acalypha indica* var. *bailloniana* (Müll. Arg.) Hutch.; *Acalypha indica* var. indica.; *Acalypha somalensis* Pax; *Acalypha somalium* Müll. Arg.; *Acalypha spicata* Forssk.; *Cupamenis indica* (L.) Raf.; *Ricinocarpus baillonianus* (Müll. Arg.) Kuntze; *Ricinocarpus deciduus* (Forssk.) Kuntze and *Ricinocarpus indicus* (L.) Kuntze. There are two invalid synonymous names for this plant (*Acalypha canescens* Wall. and *Acalypha ciliata* Wall.) and one illegitimate name (*Acalypha caroliniana* Blanco). The accepted name to refer to this plant is *Acalypha indica* L. (The Plant List, 2013). The hierarchical taxonomy list of *Acalypha indica* had been verified by the Integrated Taxonomic Information System and the common name for this species in English is Indian copperleaf (Integrated Taxonomic Information System, 2015). This plant belongs to the Acalypha genus which is classified as the fourth largest genus in Euphorbiaceae family. Most of the plants from this family are used as medicinal herbs in Asian and African regions (Seebaluck et al., 2015).

Acalypha indica is a small annual erect herb plant that grows up to 0.6 m (Stone, 1970), 0.35–0.75 m (Kirtikar and Baman, 1918), 0.3–1.0 m (Takle et al., 2011) and is capable heights of reaching 1.5–2.5 m (Schmelzer, 2007). It is a taproot type plant and its leaves are 2.5–7.5 cm long with 2.0–4.5 cm broad either ovulate or rhombic ovulate shape. The leaves have acute or sub obtuse crenate-serrate, glabrous thin and base cuneate as shown in Fig. 2(A). Their petiolate is usually longer than the blade, slender, and stipulate minute (Kirtikar and Baman, 1918; Stone, 1970). The leaves of the *Acalypha indica* are simple and arranged spirally; 0.02–12.00 cm petiole long; blade broadly ovate to ovate-lanceolate; 2–9 cm × 1–5 cm; base cuneate; apex acute; margins toothed; membranous; sparingly short hairs to almost glabrous is nature on both surfaces; more hairy along the midrib; 5-veined at base and with 4–5 pairs of lateral veins (Schmelzer, 2007). One month after germination, the stem starts to turn woody as it matures. The stem is sparing to densely hairy (Schmelzer, 2007). The branches are numerous, long, ascending, and finely pubescent (Saha and Ahmed, 2011b).

The flower of the *Acalypha indica* is arranged in numerous lax, erect, elongated, auxiliary spikes, and clusters near the summit of the spikes as shown in Fig. 2(B). The female is in white color, scattered, and surrounded by a shortly pedunculate large leafy dentate cuneiform with many nerves bract that is approximately 6–8 mm in diameter (Kirtikar and Baman, 1918). The flowers are sessile on erect axillary spikes longer than the leaf. The male flowers are minute and crowded distally with 8 stamens, while the female flowers are scattered along inflorescence axis, each is subtended by a conspicuous semicopula foliaceous toothed green bract, nearly 7 mm long (Stone, 1970). The

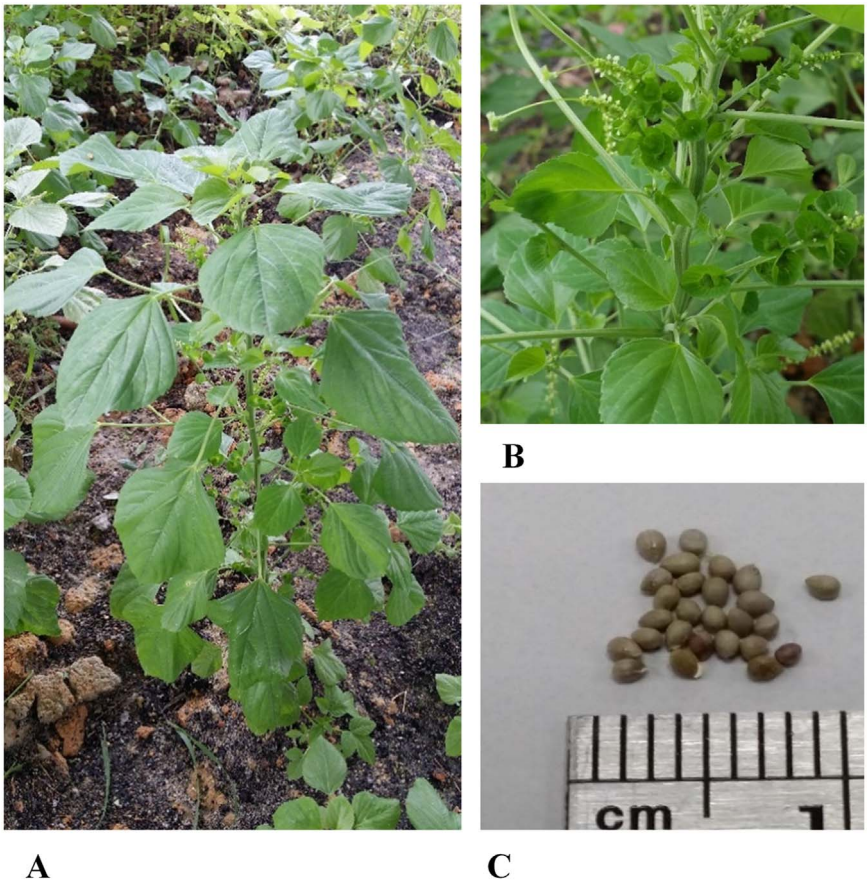

Fig. 2. *Acalypha indica*: (A) whole plant, (B) stem and flowers and (C) seeds.

inflorescences are in axillary, solitary or paired spike reaching up to 6–10 cm long. The lower 75% comprises of laxly arranged female flowers and the upper part with densely congested male flowers that are usually terminated by a female flower; bracts in female flowers transversely ovate to almost orbicular, 0.5–1 cm × 1–1.5 cm, toothed, each subtending 1–2 or 5 flowers. The flowers are unisexual, sessile and petals absent; male flowers with 4-lobed, minute, granular dotted, greenish calyx and stamens 8; female flowers with 3 triangular-ovate, ciliate sepals, ovary superior, 3-celled, slightly 3-lobed, styles 3, fused at base and fringed (Schmelzer, 2007). The fruits of the *Acalypha indica* are small and hairy. The seeds are minute, ovoid in shape and pale brown in color. The capsules are small, hispid, and quite concealed by the bract (Nadakarni and Nadakarni, 1982). The fruit is a 3-lobed capsule with 1.5 mm × 2.0 mm, granular dotted, short-hairy, splitting into 3 cocci, each 2-valved and 1-seeded. The seeds are ovoid, c. 1.5 mm × 1.0 mm, smooth, gray, caruncle linear and appressed with the terminal flower producing 1 seed (Schmelzer, 2007). In the early stages of seed formation, its color changes from greenish white into a completely brownish or gray color depending on its maturity. Fig. 2(C) shows the mature seed of *Acalypha indica*.

Khrisnan et al. (2000) reported the optimum growth of *Acalypha indica* can be achieved when the plant is located on top of the hill with 550 m height from sea level. This information was obtained by comparing six plant morphological parameters from different height locations of the hill; top (550 m), middle (350 m) and foot (275 m). The quantity of leaves quantities and plant height had increased when they received massive amounts of water from rain during the monsoon season rather than the summer season (Khrisnan et al., 2000).

2.2. Distribution

Acalypha indica grows naturally in wet, temperate, and tropical areas along the equator cross-continental of Asian, Africa, Europe, South and North America and Australia as shown in Fig. 1. The Discoverlife (2015) database reported the spread distribution of *Acalypha indica* in the most wet and warm tropical regions especially in Asia, from t India to Australia. The Indian people have the most documented records of plant utilization for their traditional medicines (Martin, 1995; Savithramma et al., 2007). Meanwhile, many Australians recognized this plant in their area but are less inclined to consume it (Scaffidi et al., 2016). *Acalypha indica* also can be found in the Arabia Gulf region based on the report that they consumed this plant as a food (Marwah et al., 2007). *Acalypha indica* is also a common weed found in south Nigeria and West Africa (Burkill, 1994). Schmelzer (2007) reports levels of high distribution particularly in Africa from the central part of equator down to the southern of Africa through Ethiopia, Sudan, DR Congo, South Africa, Somalia, Kenya, Mozambique, Tanzania, Zambia, Nigeria and others.

2.3. Vernacular names

Since *Acalypha indica* grows in many areas around the world, each local people have a specific name for this plant as listed in Table 1. Some countries like India, Malaysia, Indonesia, Thailand, and others have more than one name depending on local accents, ethnics, and races in those countries. European countries like Britain, Spain, France, and Germany have their own name for this plant; however, they may not consume this plant as other people in Asia and Africa do. The local name of *Acalypha indica* in Bangladesh and Sri Lanka is similar to the vernacular name in India, because of the historical factor in people migration in South Asia. The ethnicities from these countries were distributed a long time ago before modern boundaries were introduced. Most vernacular names are reported in India country as shown in Table 2. The Indian people comprise of many ethnicities that

Table 1
Local name of *Acalypha indica* in other countries.

Local name	Country	Refs.
Muktajhuri	Bangladesh	Das et al. (2012), Mucignat-Caretta et al. (2014)
Alcalifa	Brazil	Dineshkumar et al. (2010), Ocktarini (2010), Ranju et al. (2011), Saha and Ahmed (2011b)
English Indian Acalypha, Indian Nettle, Three-Seeded Mercury	Britain	Dineshkumar et al. (2010), Ranju et al. (2011), Schmelzer (2007)
Tie Xian	China	Ocktarini (2010)
Horrisa	Djibouti	Aboubaker et al. (2013)
Baro, Berbere	Ethiopia	Giday and Teklehaymanot (2013)
Ricinelle Des Indes, Oreille De Chatte, Herba Chatte	France	Schmelzer (2007)
Indisches Brennkraut	German	Dineshkumar et al. (2010), Ranju et al. (2011), Saha and Ahmed (2011b)
Kuppaimeni	India	Dineshkumar et al. (2010), Ranju et al. (2011), Walter (2007)
Anting-anting, Lelatang, Rumput Kosongan (Sunda), Kucing-kucingan, Rumput Bolong-bolong (Java), Akar Kucing	Indonesia	Andries (2009), Ocktarini (2010), Saha and Ahmed (2011b)
Kucing Galak, Lis-lis, Cheka Emas	Malaysia	Andries (2009), Ocktarini (2010), Saha and Ahmed (2011b), Vimala (2013)
Maraotong, Bugos, Taptapingar	Philippines	Andries (2009), Ocktarini (2010)
Mukta barshi jhar	Nepal	Singh et al. (2012)
Ntlambissana	Mozambique	Ribeiro et al. (2010)
Ricinela	Spain	Dineshkumar et al. (2010), Ranju et al. (2011), Saha and Ahmed (2011b)
Kuppameniya	Sri Lanka	Kankanamalage et al. (2014)
Tamyae Tuaphuu, Tamyae Maeo, Haan Maeo	Thailand	Andries (2009), Saha and Ahmed (2011b)
Tai Tuw Owjng Aasn, Tai Tuw Ownjng Xanh	Vietnam	Andries (2009)

use multiple languages in their conversations. Since most Indian people practice Ayurveda for conventional medicinal treatments, they always consume any available plant existing around them as a medicine source including *Acalypha indica* (Dineshkumar et al., 2010).

3. Ethnomedicinal practices

Most of the practices come from people in the Asian and African regions as shown in Table 3. Some people in India are a regular consumers of this plant since it is part of the Ayurveda practice. Meanwhile, other countries use this plant as part of their treatment but usage is minimal. The implementation of *Acalypha indica* plant for ethnomedicinal purposes can be divided into three main parts; whole plant, leaves and roots. The method of applying this plant for treatment as a single use or in a combination with other ingredients also plays an important role and needs to be discussed. The plant condition during treatment, fresh or dry, could also be an important factor in its therapeutic effectiveness. Even though the plant is known for its therapeutic purposes, there are some people who consume this plant as a food prepared either as a green leafy vegetable or a fried flour snack in their daily meal (Schmelzer, 2007).

64% of ethnomedicinal practices consume the leaf parts of the plant, followed by the whole plant (24%) and the root (12%) as shown in Fig. 3(A). The leaves are the most abundant part and easy to be separated, compared to the root, stem, seeds, and flowers. The leaves of the *Acalypha indica* can be used to induce an abortion (Kumar et al., 2012), as an anthelmintic (Mohan et al., 2012), for asthma (Savithramma et al., 2007), for diarrhea (Das et al., 2012), as an emetic (Ghani, 2003; Mohan et al., 2012), as a laxative (Ribeiro et al., 2010), for rheumatoid arthritis (Singh et al., 2012), syphilitic ulcer (Jayaprakasam and Ravi, 2013) and wound healing (Marwah et al., 2007). There are two oral methods to consume the leaves which are in a leaves decoction or eaten raw. Besides, this plant also can be used for external therapeutic applications such as constipation (Saha et al., 2011b), dermatology ailment (Ameenah Gurib-Fakim and Guého, 1996; Gurib-Fakim, 2011; Lingaraju et al., 2013; Mutheeswaran et al., 2011; Paindla and Mamidala, 2014; Rampilla and Mahammad, 2015; Rastogi and Mehrotra, 1990; Seebaluck et al., 2015; Steyn, 1938), ear ache (Jayaprakasam and Ravi, 2013; Mohan et al., 2012; Seebaluck et al., 2015), epilepsy (Henry et al., 1996; Reddy et al., 2010; Sharma et al., 2013), ganglion (Aboubaker et al., 2013), gum and teeth disease (Divya et al., 2014), headache (Saha et al., 2011b), hemorrhoids (Ribeiro et al., 2010), insect bites (Kirtikar and Baman, 1918; Nadakarni, 1982), pimples (Malaysia Peninsular Forestry Department,

Table 2
Vernacular names of *Acalypha indica* in Indian ethnics.

Vernacular names	Ethnic language	Refs.
Muktajhuri, Sveta-basanta	Bengali	Ranju et al. (2011), Walter (2007)
Vanchi Kanto	Gujarat	Dineshkumar et al. (2010), Ranju et al. (2011), Walter (2007)
Kuppu, Khokali	Hindi	Dineshkumar et al. (2010), Ranju et al. (2011), Ved et al. (2016), Walter (2007)
Kuppigida	Kannada	Ved et al. (2016), Walter (2007)
Kunkmiphal	Konkani	Walter (2007)
Kuppamani	Malayalam	Dineshkumar et al. (2010), Ved et al. (2016), Walter (2007)
Khajoti, Khojoti, Khokalee, Khokali, Khokla, Khokli, Kupameni, Kupi, Kuppi, Mamjarshejari, Petari, Pitari, Shendri	Marathi	Ved et al. (2016)
Arittamanjarie	Sanskrit	Dineshkumar et al. (2010), Ranju et al. (2011), Ved et al. (2016), Walter (2007)
Kupa-menya	Sinb	Dineshkumar et al. (2010), Walter (2007)
Kuppsamenia	Sinhalese	Dineshkumar et al. (2010)
Kuppivaeni, Kuppaimeni	Tamil	Dineshkumar et al. (2010), Ranju et al. (2011), Ved et al. (2016), Walter (2007)
Kuppichettu, Harita-manjiri, Kuppinta, Muripindi	Telugu	Dineshkumar et al. (2010), Ranju et al. (2011), Ved et al. (2016), Walter (2007)
Indramaris	Uriya	Dineshkumar et al. (2010), Ranju et al. (2011), Walter (2007)

Table 3
Ethnomedicinal practices of *Acalypha indica*.

Uses	Plant part (s) used/Implementation	Country practiced	Refs.
Abortion	Leaves	India	Kumar et al. (2012)
Anthelmintic	1. Leaf paste with lime juice 2. Powder of dry leaves 3. Decoction with garlic	India	Mohan et al. (2012)
Anti-parasite	Leaves are ground with either common salt, quicklime or lime juice for external uses	India	Mohan et al. (2012)
Aphrodisiac	Dried leaves decoction	Malaysia	Vimala (2013)
Asthma	Decoction, 50 ml taken per day, for 1 week by mouth	India	Savithramma et al. (2007)
Bronchitis	Whole plant is crushed and the juice is applied	India	Senthilkumar et al. (2006)
Constipation	Leaves ground into a paste and made into a ball-shape. The paste is introduced into the rectum to relax the sphincter and produces relief motions	India	Saha and Ahmed (2011b)
Dermatology ailment	1. Leaves 2. Dried leaves poultice 3. Leaf juice is prepared with either oil or lime	India	Paindla and Mamidala (2014) Steyn (1938) Lingaraju et al. (2013)
	Leafs juice	India	Paindla and Mamidala (2014)
	Paste is prepared by using nine leaves of *Acalypha indica* and pepper to the two gram size tablet. Paste is prepared by using leaves and black cuminum then applied as a balm.	India	Rampilla and Mahammad (2015)
	Crush leaves poultice is mixed with *Cardiospermum halicacabum*	Mauritius	Ameenah Gurib-Fakim and Guého (1996), Gurib-Fakim (2011), Lingaraju et al. (2013), Mutheeswaran et al. (2011), Rastogi and Mehrotra (1990), Seebaluck et al. (2015)
Diarrhea	Leaves, roots and seeds	Bangladesh	Das et al. (2012)
Ear ache	Leaf decoction	India	Jayaprakasam and Ravi (2013), Mohan et al. (2012), Seebaluck et al. (2015)
	Whole plant decoction given orally	Nepal	Singh et al. (2012)
Emetic	Leaf juices	India	Ghani (2003), Mohan et al. (2012)
Emmenagogue	Whole plant	India	Kumar et al. (2012), Nadakarni and Nadakarni (1982)
Epilepsy	Leaves ground with garlic, pepper and leaves of *Leucas aspera*, extract given orally	India	Reddy et al. (2010), Sharma et al. (2013)
	Leaves mixed with *Cardiospermum halicacabum* and boiled in *Azadirachta indica* oil. Extract is consumed	India	Henry et al. (1996), Sharma et al. (2013)
Expectorant	Whole plant	India	Jayaprakasam and Ravi (2013)
Fever	Root	India	Rastogi and Mehrotra (1990)
Ganglion	Leaf paste is applied	Djibouti	Aboubaker et al. (2013)
Gum and teeth disease	Powder or decoction	India	Divya et al. (2014)
	Whole plant decoction given orally	Nepal	Singh et al. (2012)
Headache	Leaf decoction	India	Jayaprakasam and Ravi (2013)
	In congestive headache, a piece of cotton saturated with the pressed juice of the plant or leaves is inserted into each nostril. They say it can relieve a headache by causing a hemorrhage from the nose.	India	Saha and Ahmed (2011b)
Hemorrhoids	Crushing and leaf decoction	Mozambique	Ribeiro et al. (2010)
Insect bites	Leaf poultice	India	Kirtikar and Baman (1918), Nadakarni and Nadakarni (1982)
Laxative	Root infusion	India, Malaysia	Mohan et al. (2012), Nadakarni and Nadakarni (1982), Vimala (2013)
	Grinding, decoction and maceration	Mozambique	Ribeiro et al. (2010)
Lowered Blood Sugar	Root extract	India	Chopra et al. (1956)
Mouth ulcer	Whole plant decoction	Malaysia	Vimala (2013)
	Whole plant decoction	Malaysia	Malaysia Peninsular Forestry Department (2017)
Pimples	Leaves are ground with ginger	Malaysia	Malaysia Peninsular Forestry Department (2017)
Rheumatoid arthritis	Fresh leaf juice	Nepal	Singh et al. (2012)
Syphilitic ulcer	Leaf decoction	India	Jayaprakasam and Ravi (2013)
Wound healing	Blend with *Ficus benghalensis*, *Morus alba* and *Tridax procumbens*	India	Basha and Sudarshanam (2011)
	Eat	Oman	Marwah et al. (2007)

2017) and wound healing (Basha and Sudarshanam, 2011; Jayaprakasam and Ravi, 2013).

In some practices in India, the whole plant is consumed. They use the whole plant instead of the leaves to cure bronchitis by crushing the plant for fresh juice (Senthilkumar et al., 2006). The whole plant is also beneficial in treating ear aches and oral diseases in Nepal (Singh et al., 2012), expectorant in India (Jayaprakasam and Ravi, 2013) and mouth ulcers in Malaysia (Malaysia Peninsular Forestry Department, 2017; Vimala, 2013). In Malaysia, the whole and dry *Acalypha indica* plant is served as a tea beverage for aphrodisiac purposes (Vimala, 2013). Few people use the root decoction for treating some illnesses like diarrhea (Das et al., 2012), fever (Rastogi and Mehrotra, 1990), as a laxative (Mohan et al., 2012; Nadakarni, 1982; Vimala, 2013) and for low blood sugar (Chopra et al., 1956) in their practices. Notably, each part of this plant has certain functions for therapeutic properties based on ethnomedicinal practices. Therefore, further scientific study is required to investigate its performance during treatment.

Some people mix this plant with other ingredients or remedies to enhance the treatment efficiency on a disease. Approximately 58% of practices prefer to combine this plant with another herb to increase the effect as shown in Fig. 3(B). For example, the people in India use *Acalypha indica* leaves with lime juice or garlic for anthelmintic treatment (Mohan et al., 2012). Meanwhile, the leaves can be mixed together with oil and other herbs such as black cuminum and

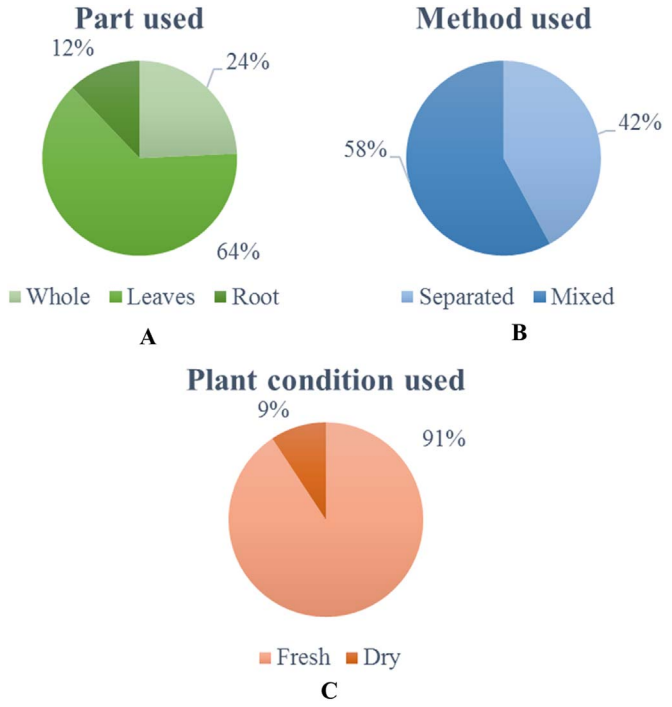

Fig. 3. (A) Percentage of plant part used, (B) method used and (C) plant condition used from *Acalypha indica* in ethnomedicinal practice adopted from Table 3.

Cardiospermum halicacabum for external application to treat any disease related to skin ailment (Ameenah Gurib-Fakim and Guého, 1996; Gurib-Fakim, 2011; Lingaraju et al., 2013; Mutheeswaran et al., 2011; Rampilla and Mahammad, 2015; Rastogi and Mehrotra, 1990; Seebaluck et al., 2015). A similar treatment process with different herbs (*Leucas aspera*, *Cardiospermum halicacabum* and *Azadirachta indica* oil) is used by people in India) to treat epilepsy (Henry et al., 1996; Reddy et al., 2010; Sharma et al., 2013).

The ethnomedicinal practices more commonly involve *Acalypha indica* (91%) rather than the dry form (9%) as presented in Fig. 3(C). The fresh plant contains completely natural phytochemicals that are useful for all therapeutic activities including fatty acid, volatile compound and essential oil. From observing ethnomedicinal practices, it was found that the volatile compound might be responsible for the therapeutic activities. The fresh *Acalypha indica* leaves produce a strong smell during the drying process showing the presence of volatile compounds from evaporation. A weight loss of 80% after the drying process demonstrates the high moisture content and volatile compound of this plant. Nevertheless, the remaining phytochemicals in the dry plant are beneficial in curing other therapeutic problems such as anthelmintic (Mohan et al., 2012), skin problems (Steyn, 1938) oral diseases (Divya et al., 2014), and act as an aphrodisiac (Vimala, 2013).

The application of *Acalypha indica* in ethnomedicinal practices mostly occurs in Asian and African regions, and even though this plant grows in wet, hot, and temperate tropical climate, there are no records found outside either region. Many local places list this plant in their database archives but not many people use this plant as medicine. The optimum use of this plant is varied based on the location and local knowledge of practices. This plant may be also taken as a means of dieting when consumed as a leafy green vegetable rather than in medicinal application like people in India and Oman (Marwah et al., 2007; Schmelzer, 2007). In Malaysia, some manufacturers process the dry leaves of this plant and sell it to the public as a healthy drink (Malaysiakini, 2006); who also believe this plant can be used to stimulate their libido, especially for men. However, until now there has been no scientific evidence to prove this claim and the people are relying on the information given by their ancestors.

Acalypha indica also can be used to treat insect bites (Kirtikar and Baman, 1918; Nadakarni, 1982). Insect bites causes inflammation of the skin, blisters and irritation depending on the types of poison released during the sting. Since *Acalypha indica* can cure ailments related to the skin, it is also applied to insect bites to reduce soreness. The leaves also contain good anti-bacterial activity, anti-fungal activity and antioxidant phytochemicals which are useful in protecting the skin from external hazards. The released fluid from crushed leaves is useful as a lubricant for child constipation treatment by applying the small ball-shaped made from leaves into the rectum. Additionally, the fluid is composed of an oily compound to loosen the rectum for feces release and protect the wounded rectum wall. An adult with hemorrhoids can also use this fluid by rubbing it around the rectum. The phytochemicals inside this plant can treat and contract the hemorrhoids through wound healing activities. Furthermore, the fresh leaves possess a high amount of volatile chemicals to treat headaches, epilepsy, ear aches and as an expectorant. Since *Acalypha indica* has an anti-bacterial properties, wound healing activities, is edible and safe to consume, people prefer to use this plant to treat sickness related to gum and teeth.

4. Phytochemical study

4.1. Phytochemical and nutrient constituent of Acalypha indica

The fresh *Acalypha indica* plant has a wide variety nutrients such as carbohydrates, proteins, vitamins, and fat as shown in Table 4

Table 4
Nutritional composition of *Acalypha indica*.

Nutritional	Values	Refs.
Ash	159,000 ppm	Duke (2016)
Acid insoluble ash	0.58%	Takle et al. (2011)
Arsenic, As	0.95×10^{-1} ppm	Moscow and Jothivenkatachalam (2012)
Cadmium, Cd	6.25×10^{-3} ppm	Moscow and Jothivenkatachalam (2012)
Calcium, Ca	66.7 ppm	Schmelzer (2007)
	34,205 ppm	Duke (2016)
Calcium oxalate	–	Duke (2016)
Carbohydrate	6 g per 100 g	Schmelzer (2007)
	300,700 ppm	Duke (2016)
Chromium, Cr	4.65 ppm	Moscow and Jothivenkatachalam (2012)
Copper, Cu	9.65 ppm	Moscow and Jothivenkatachalam (2012)
Energy	269 kJ per 100 g	Schmelzer (2007)
Fat	1.4 g per 100 g	Schmelzer (2007)
	71,800 ppm	Duke (2016)
Ferum, Fe	156.59 ppm	Moscow and Jothivenkatachalam (2012)
	885 ppm	Duke (2016)
Fibre	2.3 g per 100 g	Schmelzer (2007)
	23,000 ppm	Duke (2016)
Lead, Pb	0.82 ppm	Moscow and Jothivenkatachalam (2012)
Mercury, Hg	0.35×10^{-2} ppm	Moscow and Jothivenkatachalam (2012)
Moisture content	80%	Schmelzer (2007)
Nickel, Ni	4.35 ppm	Moscow and Jothivenkatachalam (2012)
Phosphorus, P	9.9 ppm	Schmelzer (2007)
	5075 ppm	Duke (2016)
Protein	6.7 g per 100 g	Schmelzer (2007)
	343,590 ppm	Duke (2016)
Sulphate ash	26%	Takle et al. (2011)
Total ash	16%	Takle et al. (2011)
Vitamin C	14.7 ppm	Duke (2016), Schmelzer (2007)
Water soluble ash	2.33%	Takle et al. (2011)
Water	805,000 ppm	Duke (2016)
Zinc, Zn	47.18 ppm	Moscow and Jothivenkatachalam (2012)

Table 5
Phytochemical content in *Acalypha indica* from the whole plant, leaf, root, flower, and unstated part.

Phytochemical	Plant part	Refs.
Acaindinin	Whole plant	Ma et al. (1997)
Acalyphamide	Whole plant	Duke (2016)
	Unstated	Ghani (2003), Talapatra et al. (1981)
Acetonylgeraniin	Whole plant	Ma et al. (1997)
Aurantiamide	Leaf	Raj and Singh (2000)
	Whole plant	Duke (2016)
	Unstated	Talapatra et al. (1981)
Caffeic acid	Leaf	Murugan and Selva (2015)
Catechol	Unstated	Chitravadivu et al. (2009)
Chebulagic acid	Unstated	Ma et al. (1997)
Clotrisiloxane, Hexamathyl-	Leaf	Selvamani and Balamurugan (2015b)
Corilagin	Whole plant	Ma et al. (1997)
Cyanogenic glucoside – acalyphine, acalyphin amide, epiacalyphin, epinoracalyphin, epiacalyphin amide cycloside, *ar*-acalyphidone, noracalyphin, *seco*-acalyphin	Leaf	Azmahani et al. (2002)
	Whole plant	Duke (2016), Raj and Singh (2000)
	Unstated	Ghani (2003), Hungeling et al. (2009), Nahrstedt et al. (1982), Ranju et al. (2011)
Cysteine	Whole plant	Hussain and Kumaresan (2013)
Ellagic acid	Unstated	Joy et al. (2010)
Flavonoid – Chrysin, hesperetin, galangin, kaempferol (Biorobin, clitorin, mauritianin, nicotiflorin), naringin, naringenin, quercetin (Rutin), quercetin 3–0-β-D-glucoside	Leaf and flower	Ma et al. (1997), Murugan and Selva (2015), Nahrstedt et al. (2006)
	Whole plant	Duke (2016), Hussain and Kumaresan (2013), Raj and Singh (2000)
	Unstated	Ghani (2003), Hiremath et al. (1998), Joy et al. (2010), Ma et al. (1997), Nahrstedt et al. (2006), Purushothaman et al. (1973), Suri et al. (2004)
Flindersin	Unstated	Taufiq-Yap et al. (2000)
Ferulic acid	Leaf	Murugan and Selva (2015)
Gallic acid	Leaf	Joy et al. (2010), Ma et al. (1997), Murugan and Selva (2015)
Geranin	Whole plant	Ma et al. (1997)
Glucogallin	Whole plant	Ma et al. (1997)
Hydrogen cyanide	Leaf	Duke (2016)
Inositol methyl ether	Leaf	Azmahani et al. (2002); Duke (2016)
Kaur-en-18-oic acid	Unstated	Joy et al. (2010)
N-methyl-3-cyanopyridones	Whole plant	Duke (2016)
Phenol, 24 BIS(1,1-Dimethylethyl)	Leaf	Selvamani and Balamurugan (2015b)
Potassium Brevifolin carboxylate	Whole plant	Ma et al. (1997)
Proline, 3,4-didehydro-	Leaf	Mohan et al. (2012)
	Whole plant	Hussain and Kumaresan (2013)
Propanenitrile,3- (5-diethylamino-1-methyl-3-pentynyloxy)	Leaf	Mohan et al. (2012)
	Whole plant	Hussain and Kumaresan (2013)
Quebrachitol	Whole plant	Duke (2016), Raj and Singh (2000)
	Unstated	Sanseera et al. (2012)
Quinine	Unstated	Ghani (2003)
Repandusinic acid	Unstated	Ma et al. (1997)
Resin	Leaf	Azmahani et al. (2002)
	Whole plant	Duke (2016)
	Unstated	Ghani (2003)
Stigmasterol	Root	Raj and Singh (2000)
	Unstated	Ghani (2003)
Succinimide	Leaf	Raj and Singh (2000)
	Whole plant	Duke (2016)
	Unstated	Talapatra et al. (1981)
Syringic acid	Leaf	Murugan and Selva (2015)
Tannin	Whole plant	Duke (2016), Raj and Singh (2000)
	Unstated	Ghani (2003), Ma et al. (1997), Purushothaman et al. (1973)
Tectoquinone	Whole plant	Duke (2016)
Triacetonamine	Leaf	Azmahani et al. (2002)
	Whole plant	Duke (2016), Raj and Singh (2000)
	Unstated	Ghani (2003)
Trimethy [4-(1,1,3,3, Tetramethylbutyl) phenox] Silane	Leaf	Selvamani and Balamurugan (2015b)
Tri-O-methylellagic acid	Leaf	Raj and Singh (2000)
	Whole plant	Duke (2016)
	Unstated	Ghani (2003)
β-sitosterol acetate	Whole plant	Duke (2016), Raj and Singh (2000)
β-Sitosterol ß-D-glucoside	Leaf	Raj and Singh (2000)
	Whole plant	Duke (2016)
γ-Sitosterol	Unstated	Ghani (2003)
γ-Sitosterol acetate	Whole plant	Duke (2016)
1,2,3,6-tetra-O-galloyl-β-D-glucose	Whole plant	Ma et al. (1997)
1,3-Dioxolane, 4-Ethyl-5-Octyl-2,2-Bis (Trifluoromethyl)-, Trans-	Leaf	Selvamani and Balamurugan (2015b)
1H-Pyrrole-2,5-dione, 1-ethenyl	Leaf	Mohan et al. (2012)
	Whole plant	Hussain and Kumaresan (2013)
16 α, 17-dihydroxy-*ent*-kauran 19-oic acid	Unstated	Joy et al. (2010)
2-methyl anthraquinone	Leaf	Duke (2016), Raj and Singh (2000)
	Unstated	Ghani (2003), Selvamani and Balamurugan (2015b)

(continued on next page)

Table 5 *(continued)*

Phytochemical	Plant part	Refs.
3,3′ Methylene bis (4-hydroxyl coumarin)	Leaf	Murugan and Selva (2015)
3,8-Nonadien-2-one, E	Leaf	Mohan et al. (2012)
	Whole plant	Hussain and Kumaresan (2013)
-4,4′,5,5′,6,6′ hexahydroxy diphenic acid	Unstated	Joy et al. (2010)
4-Amino-3-methoxypyrazolo[3,4-*d*] pyrimidine	Leaf	Mohan et al. (2012)
	Whole plant	Hussain and Kumaresan (2013)

(Duke, 2016; Schmelzer, 2007). This plant also contains mineral micronutrients as supported by Moscow and Jothivenkatachalam (2012). They decided to prepare its documentation with detailed evidence of essential and non-essential heavy metals content as a part of the herbal standardization preparation. *Acalypha indica* has a high iron content, followed by zinc, copper, nickel and chromium which are useful for patients with mineral deficiencies problems. This plant has a high moisture content of up to 80% and a total ashes value of 16% (Schmelzer, 2007; Takle et al., 2011) suitable for body hydration. As a leafy low-cost vegetable, this plant can provide a good balance in nutrients at minimal costs.

Researchers have studied and listed the phytochemicals in *Acalypha indica* from plant parts as shown in Table 5. These studies show some relevance in the interrelationship between ethnomedicinal practices with the respective parts of the plant. Ma et al. (1997) reported the list of phenolic compounds derived from this plant and discovered that phenolic phytochemicals like geraniin, corilagin, chebulagic acid and glucogallin were useful as antioxidants. Meanwhile, Joy et al. (2010) stated that there were five compounds from the ethanolic extract of the leaves which acted as antioxidants. Ellagic acid, gallic acid, kaur-en-18-oic-acid, 16 α,17-dihyroxy-*ent*-kauran 19-oic-acid and 4,4′,5,5′,6,6′ hexahydroxy diphenic acid, can be found inside this plant. Sanseera et al. (2012) indicated active inhibition of anti-cancer activity against small cell lung cancer by the quebrachitol compound found inside leaves. This compound is responsible for healing respiratory problems such as asthma and bronchitis as shown in Table 3. Furthermore, the stigmasterol compound in *Acalypha indica* is beneficial for specific hormone stimulation that plays an important physiological role in regulating and rebuilding tissues (Sundararaman et al., 1977). This compound might be used as an energy booster for sexual health in men; it is used in Malaysia as an aphrodisiac.

There are several flavonoids detected in *Acalypha indica* leaves which are useful for many therapeutic activities like anti-bacterial, antioxidant, anti-fungal, anti-ulcer, etc. (Duke, 2016; Ghani, 2003; Hiremath et al., 1998; Hussain and Kumaresan, 2013; Joy et al., 2010; Ma et al., 1997; Murugan and Selva, 2015; Nahrstedt et al., 2006; Purushothaman et al., 1973; Raj and Singh, 2000; Suri et al., 2004). Although Nahrstedt et al. (2006) claimed some flavonoids were undetected in their study according to previous studies like chrysin and hesperitin, there could be several factors that affect the sample during the analysis. Both the type of ethnomedicine being practiced and the analysis results can also be affected by the geographical location (Guo et al., 2011). Despite the beneficial compounds, *Acalypha indica* also contains cyanogenic glycoside which is harmful and lethal to humans (Azmahani et al., 2002; Duke, 2016; Ghani, 2003; Hungeling et al., 2009; Nahrstedt et al., 1982; Ranju et al., 2011). Reflecting on this issue, since *Acalypha indica* is a weed, it needs a defence mechanism to survive and protect itself from herbivores. Therefore, the presence of cyanogenic compound can ward off herbivores and increase its chance of survival in the wildlife (Francisco et al., 2000). The other known phytochemicals are listed in Table 5, as additional information for future studies related to this plant.

Acalypha indica also has a high phenolic content, especially in ethyl acetate extraction of 7.21 mg/GAE (Gallic Acid Equivalent) followed by extraction using methanol, ethanol and hexane with 2.11, 1.63 and 1.45 mg/GAE, respectively (Pragada et al., 2011). The phenolic compound is useful and plays a major role in many human therapeutic properties (Pragada et al., 2011). There is a study reporting the total protein content inside *Acalypha indica* leaves by Devi and Raj (2013). The quantity of protein content inside the leaves is 0.0025 mg/ml with 19 kDa, protein fraction value (Devi and Raj, 2013). Based on the current review so far, only three studies represent a phytochemical analysis on *Acalypha indica* leaves using Gas chromatography–mass spectrometry which comprised of methanolic extraction (Hussain and Kumaresan, 2013), ethanolic extraction (Mohan et al., 2012) and acetone extraction (Selvamani and Balamurugan, 2015b). From the GCMS analysis of methanolic and ethanolic extracts, five identical compounds were detected that may be responsible for all the therapeutic activities discussed in Section 5; these include1H-Pyrrole-2,5-dione, 1-ethenyl; 3,8-Nonadien-2-one, E; Proline, 3,4-didehydro-; 4-Amino-3-methoxypyrazolo[3,4-*d*] pyrimidine; and Propanenitrile,3-(5-diethylamino-1-methyl-3-pentynyloxy).

4.2. Phytochemical constituent of fatty acids and volatile oils in *Acalypha indica*

Acalypha indica leaves have some amount of volatile oil and release quite a strong odor when evaporating. The presence of a volatile oil could be another mechanism for survival in the wildlife (Isman, 2000). It consists of a complex mixture of phytochemicals like terpene and terpenoid as reported by Andries (2009). Suri et al. (2004) took the initiative to analyze the content of the volatile oil and fatty acid in this plant and have identified several major compounds as shown in Table 6. For the volatile oil analysis, the major compounds are trans-phytol, hexenol and decane with 39%, 18% and 10%, respectively. The hexenol is the leaf's alcohol that produces a strong odor; it is used to attract or repel insects (Wei et al., 2011). The insect will be attracted to the plant and eat the leaves that contain the cyanogenic compound, which results in cyanide intoxicated as the plant provides a natural, biological trap for pesticide control. From the fatty analysis, the major compounds are eicosatrienoic acid methyl ester, hexatriacontane, trifluoro acetic acid and n-heptadecyl ester with 35.0%, 9.6% and 8.9%, respectively. The n-octacosanol found in the fatty acids of *Acalypha indica* is useful for inhibiting cholesterol production (Taylor et al., 2003).

5. Pharmacological

5.1. Introduction

Several past reviews by other researchers have listed information related to the compilation of the plants application with its therapeutic properties and pharmacological activities (Dineshkumar et al., 2010; Mutheeswaran et al., 2011; Saha et al., 2011b; Walter, 2007). Therefore, this review is intended to summarize and update all current studies regarding this plant including its applications, phytochemical content, therapeutic properties, and identification of future possible research.

To this day, ten major solvent extractors have been used for phytochemical extraction. The extractions were performed accordingly from low to high polarity index solvent; hexane, petroleum ether,

Table 6
Fatty acids and volatile oils composition in *Acalypha indica*.

Fatty acids and volatile oils	Values	Refs.
Fatty acids		
Eicosatrienoic acid methyl ester	35.47%	Suri et al. (2004)
Ethyl tetradecane	0.43%	Suri et al. (2004)
Hexadecamethyl-heptasiloxane	2.89%	Suri et al. (2004)
Hexadecanoic acid methyl ester	5.02%	Suri et al. (2004)
Hexatriacontane	9.56%	Suri et al. (2004)
Methyl arachate	0.65%	Suri et al. (2004)
n-octacosanol	Unstated	Duke (2016), Ghani (2003), Raj and Singh (2000)
Octadecane	1.54%	Suri et al. (2004)
Tetradecen-1-ol	0.81%	Suri et al. (2004)
Trifluoro acetic acid, n-heptadecyl ester	8.92%	Suri et al. (2004)
Trifluoro acetic acid, n-octadecyl ester	0.73%	Suri et al. (2004)
2,6,10 trimethyl undecatriene	8.69%	Suri et al. (2004)
2-methyl pentadecane	4.64%	Suri et al. (2004)
2-methyl tricosane	0.32%	Suri et al. (2004)
7 hexyl eicosane	0.63%	Suri et al. (2004)
7-butyl docosane	2.97%	Suri et al. (2004)
7-hexyl eicosane	6.21%	Suri et al. (2004)
Volatile oils		
Volatile oils	Unstated	Azmahani et al. (2002), Ghani (2003)
	0.01%	Suri et al. (2004)
Benzopyran	1.09%	Suri et al. (2004)
Coumaran	0.70%	Suri et al. (2004)
Decane	11.33%	Suri et al. (2004)
Hexanal	1.46%	Suri et al. (2004)
Hexenol	17.50%	Suri et al. (2004)
Isodecane	3.94%	Suri et al. (2004)
Linalool	4.13%	Suri et al. (2004)
Palmitaldehyde	2.55%	Suri et al. (2004)
Trans phytol	38.64%	Suri et al. (2004)
Tridecane	1.69%	Suri et al. (2004)
α-toaldehyde	1.09%	Suri et al. (2004)
α-tulenol	0.68%	Suri et al. (2004)
β-ionone	0.62%	Suri et al. (2004)
2-dimethyl dodecane	6.83%	Suri et al. (2004)
9,12,15 octadecatrienal	1.94%	Suri et al. (2004)

diethyl ether, ethyl acetate, chloroform, acetone, ethanol, methanol, water and mixed solvent. The plant was segmented into three parts; whole plant, top aerial and roots. As a result, the semi-polar phytochemicals from the ethanol and methanol extraction possessed the most therapeutic functions especially at the aerial part (leaves, stem, flower and seed). Major phytochemical found in this plant (any segment of the plant) has high anti-bacterial properties. There are two methods of applying the extract as practiced by researchers; these are oral and topical. A pharmacokinetic study from an oral administration is responsible for therapeutic activities such as hepatoprotective, anti-cancer, anti-hyperlipidemic, an analgesic, anti-estrogenic activity, and anti-inflammatory as a reaction with the internal body system. For a topical pharmacokinetic study, this is demonstrated by its abilities in wound healing, anti-bacterial activities and dermatology ailments.

5.2. Pharmacology activity

5.2.1. Analgesic

Acalypha indica has analgesic properties as proven by Rahman et al. (2013) by conducting in vivo study on Swiss albino mice. They used a writhing reflex method developed by Vogel (2007) to determine the analgesic activity of the *Acalypha indica* methanolic extract. Acetic acid was used to induce pain right after the extract was orally administered to the mice. The injection of acetic acid will cause trauma to the body in two phases; the first phase will release histamine and serotonin while the second phase will involve prostaglandins in the inflammatory exudates (Crunkhorn et al., 1971). Two different concentrations were tested and compared where aminopyrine was set as a positive control. The results were measured by counting the writhing induced within 10 min, immediately after the extract and standard were introduced into the mice. The 200 mg/kg and 400 mg/kg of methanolic extractions produced up to 51.1% and 57.2% of writhing inhibition, respectively. The effects exhibited adequate inhibition activities compared to the use of standard aminopyrine with a 89.9% writhing inhibition (Rahman et al., 2010). The methanolic extract disrupted the first phase of inflammation formation by inhibiting the release of histamine and serotonin. The antioxidant and anti-inflammation phytochemicals in the fresh whole plant may be responsible for this inhibition. Furthermore, the non-steroidal found in the extract also capable of inhibiting cyclooxygenase that eventually leads to the prostaglandin synthesis. From the results, *Acalypha indica* has the potential to reduce pain from inflammation and behave as a potential analgesic drug.

5.2.2. Anthelmintic activity

An anthelmintic is a drug used to expel parasitic worms that usually intrude in the human body. The parasitic worm can penetrate human and animal bodies through any available cavities like the mouth and skin. An anthelmintic drug derived from easily available herbal is encouraged since it can save costs in treatment. Certainly, the whole plant part of *Acalypha indica* has a lethal effect on the worm, according to Chengaiah et al. (2009) and Ranju et al. (2011). Both used a similar method to study the anthelmintic activity developed by Ajaiyeoba et al. (2001). From their studies, the extract from ethanol and water could kill *Pheretima posthuma* 10 min after its introduction and completely killed after 30 min. In the Chengaiah et al. (2009) study, the concentration of 50 mg/ml ethanolic root extract was dissolved and tested in a medium. The extract was lethal better than the positive control used in experiment (Albendazole 10 mg/ml) (Chengaiah et al., 2009). However, Ranju et al. (2011), who used a similar method and test subject, showed that the extract was less effective. The result of 100 mg/ml of ethanol and water extract indicated slightly less effective results than 100 mg/ml of piperazine citrate (Ranju et al., 2011). The varied results from Chengaiah et al. (2009) and Ranju et al. (2011) could possibly come from the type of positive control and concentration values used in their experiment. Chengaiah et al. (2009) stated that the extract was more lethal since the Albendazole concentration used was too small compared to Ranju et al. (2011) with the 10 folds higher concentration. In the Ranju et al. (2011) experiment, the lethal value from the extract and the standard are almost identical and contributed to the less confident results compared to Chengaiah et al. (2009). In conclusion, all parts of *Acalypha indica* have the potential to be used as a natural anthelmintic drug for the de-worming activity of the stomach. The terpenoid, flavonoid and polyphenol from the extracts are probably the sources of anthelmintic drug activity (Ranju et al., 2011). To date, nobody has conducted a study of the anthelmintic activity from this plant on actual human parasitic worms like *Ascaris lumbricoides*, *Oxyuris vermicularis* and *Ankylostomiasis*.

5.2.3. Anti-arthritis

Arthritis is a disease related to joint disorder as a result of inflammation (National Institute of Arthritis and Musculoskeletal and Skin Disease, 2014). Jayaprakasam and Ravi (2013) support the claim that the root of *Acalypha indica* from methanolic extraction has anti-arthritics properties by conducting an experiment related to anti-inflammatory activities such as the inhibition of protein denaturation, proteinase inhibitory action and anti-hyaluronidase activity. The standard drug used as a positive control in their experiment for the inhibition of protein denaturation and proteinase inhibitory action was diclofenac. The IC_{50} values for the standard in both assays were 0.04 mg/ml and 0.013 mg/ml while the methanolic extract of *Acalypha indica* was 0.052 mg/ml and 0.037 mg/ml, respectively.

The difference between the extract and the standard was not very large and was suitable for therapeutic application. For anti-hyaluronidase activity assay, the root extract exhibited 0.018 mg/ml of IC_{50} value while no other positive standards were used as a control in the assay. Hyaluronidase is an enzyme that destroys the hyaluronic acid backbone of the cartilage matrix and it is the key enzyme for rheumatoid arthritis. The elevated serum levels of hyaluronic acid is a reliable biomarker of arthritis progression in the human body (Pavelka et al., 2004).

In a separated experiment, Soruba et al. (2015) also studied proteinase inhibition and inhibition of albumin denaturation from the methanolic extract of the leaf part. 100 mg/ml of the extract exhibited 80% inhibition activity of both proteinase and albumin denaturation. The results from Jayaprakasam and Ravi (2013) and Soruba et al. (2015) verify the ethnomedicinal use by people in Nepal for treating rheumatoid arthritis disease. The whole plant is useful for treating arthritis.

5.2.4. Anti-bacterial

Most therapeutic studies that have been conducted on *Acalypha indica* are related to the anti-bacterial activities. Therefore, the authors attempt to summarize all information regarding the activity of bacteria inhibition based on those previous studies; however this has proven to be rather difficult due to the lack of information in those studies. There is conflict when identifying the inhibition method, protocol, positive and negative controls, and experiment preparation because the studies differ from one another. The classification to identify whether the extract is either active or inactive needs a justification. One of the classification methods is through measuring the diameter of the inhibition zone. From the diameter, the small number represents inactive or slightly active activity while the high number will be noted as very active (Junior et al., 2000). Then, the results are expressed in the form of inhibition percentage where between 0% and 40% it is considered weak, 41–70% is considered as active and the inhibition over 71% is very active.

Thirteen Gram-positive bacteria including Bacillus, Enterococcus, Staphylococcus and Streptococcus species have been tested from those studies as shown in Table 7. For Gram-negative bacteria only eleven bacteria were tested on the various polarity of *Acalypha indica* extractions at present. Table 8 shows the inhibition activity on Gram-negative bacteria from very active, active, weak, no inhibition, and unknown status. In conclusion for anti-bacterial activity, the fresh and raw plant approach is suggested instead of a decoction to treat diseases related to this bacterium such as pus formation and inflammation.

Specific phytochemical compounds in *Acalypha indica* responsible for bacterial inhibition are not really discussed by most researchers. They only discussed a certain group of phytochemicals in plants, which are responsible for anti-bacterial activities and do not explain the mechanism mode of inhibition. However, they are narrowing down the specific phytochemical groups involved in bacterial inhibition. The alkaloid from *Acalypha indica* is responsible for the anti-bacterial activity as explained by Batubara et al. (2016), Saranraj et al. (2010), Rajaselvam et al. (2012), and Manonmani et al. (2015). Besides, the tannin, flavonoids, polyphenol, saponin and protein also play an important role in inhibiting and retarding bacterial growth (Batubara et al., 2016; Manonmani et al., 2015; Rajaselvam et al., 2012; Saranraj et al., 2010). Other findings have revealed that organic solvents are actually involved in extracting anti-bacterial phytochemical groups from most anti-bacterial plants including *Acalypha indica* (Maji et al., 2010). In addition, most of the plants in Euphorbiaceae family usually possess anti-bacterial activities for bacteria and fungi (Awoyinka et al., 2007; Falodun et al., 2008; Peres et al., 1997). As a general conclusion, *Acalypha indica* plant is effective for use as an anti-bacterial agent. Consumption of the whole plant is recommended to treat infections while using water as a working medium is optional.

5.2.5. Anti-cancer

Acalypha indica also has the ability to become an anticancer plant as reported by Sanseera et al. (2012) and Amarnath et al. (2014). Four types of cell cancer lines have been tested against *Acalypha indica* extracts including KB-Oral cavity cancer, MCF7-breast cancer, NCI-H187-small cell lung cancer, and PC3 human prostate cell cancer. The anti-cancer activity was determined through Resazurin and MTT assay. The methanolic extract of *Acalypha indica* inhibited NCI-H187-small cell lung cancer with an inhibition concentration (IC_{50}) value of 0.025 mg/ml. Two standards have been used in the assay for comparison which were ellipticine and doxorubicin. The IC_{50} value for ellipticine and doxorubicin were 0.00088 mg/ml and 0.00005 mg/ml, respectively. The KB-Oral cavity cancer and the MCF7-breast cancer were considered unreactive with the methanolic extract since the inhibition concentration exceeded 0.05 mg/ml (Sanseera et al., 2012). Sanseera et al. (2012) claimed the quebrachitol isolated from the *Acalypha indica* as the responsible phytochemical for anti-cancer activity for NCI-H187-small cell lung cancer. In addition, a recent study has revealed that the quebrachitol could participate in several important pathways as potential anti-cancer drugs either via arrest or reverse pathways (Wang et al., 2017). For the PC3 human prostate cell cancer line, Amarnath et al. (2014) found a way to increase the effectiveness of anti-cancer activity using ethanolic extract encapsu-

Table 7
Summary of Gram-positive bacteria inhibition activity by *Acalypha indica* extracts based on solvents used.

Bacteria	Very active	Active	Weak	Inactive	Refs.
Bacillus species	M	W	–	–	Manonmani et al. (2015)
Bacillus cereus	H, C, M, EA	DE	E, W		Govindarajan et al. (2008b), Muthuvelan and Raja (2008), Samy et al. (1999), Saranraj et al. (2010)
Bacillus megaterium	EA	H, M	–	–	Pragada et al. (2011)
Bacillus subtilis	W, A	E,	EA	C	Rajaselvam et al. (2012), Saranraj et al. (2010), Somchit et al. (2010)
Enterococcus faecalis	H	–	M, E	W	Baharum (2015), Ruslan (2015)
Lactobacillus acidophilus	–	–	M	H, A	Soruba et al. (2015)
Staphylococcus species	A, E	–	–	W, M	Devi and Raj (2013), Manonmani et al. (2015)
Staphylococcus aureus	M, EA, A	H, C, DE, PE, W	E	–	Baharum (2015), Divya et al. (2014), Govindarajan et al. (2008b), Hussain and Kumaresan (2013), Mohan et al. (2012), Muthuvelan and Raja (2008), Rajaselvam et al. (2012), Ruslan (2015), Saranraj et al. (2010), Selvamani and Balamurugan (2015a), Somchit et al. (2010), Soruba et al. (2015)
Staphylococcus epidermidis	C, M, EA	H	–	–	Govindarajan et al. (2008b), Pragada et al. (2011)
Streptococcus faecalis	H, C, EA, M	–	–	–	Govindarajan et al. (2008b)
Streptococcus mutans	–	–	H, C, M	–	Batubara et al. (2016)
Streptococcus pneumoniae	–	H, DE, C	–	–	Muthuvelan and Raja (2008)
Streptococcus pyogenes	A	PE, C, EA, M	–	W	Samy et al. (1999), Selvamani and Balamurugan (2015a)

A = Acetone; C = Chloroform; E = Ethanol; EA = Ethyl acetate; DE = Diethyl ether; H = Hexane; M = Methanol; PE = Petroleum ether; W = Water.

Table 8
Summary of Gram-negative bacteria inhibition activity by *Acalypha indica* extracts based on solvents used.

Bacteria	Very active	Active	Weak	Inactive	Refs.
Aeromonas hydrophila	W	–	–	–	Muthuvelan and Raja (2008), Samy et al. (1999)
Alcaligenes viscolactis	W	–	–	–	Samy et al. (1999)
Cytophaga species	–	–	–	W	Samy et al. (1999)
Enterobacter aerogenes	EA	H, M	–	–	Pragada et al. (2011)
Enterobacter cloacae	EA	H, M	–	–	Pragada et al. (2011)
Escherichia coli	A	H, M, E, EA, PE, DE	C, W	–	Baharum (2015), Devi and Raj (2013), Govindarajan et al. (2008b), Hussain and Kumaresan (2013), Manonmani et al. (2015), Mohan et al. (2012); Muthuvelan and Raja (2008), Pragada et al. (2011), Rajaselvam et al. (2012); Ruslan (2015), Samy et al. (1999), Saranraj et al. (2010), Selvamani and Balamurugan (2015a), Solomon et al. (2005), Somchit et al. (2010), Soruba et al. (2015)
Klebsiella species	–	M, A	–	W	Manonmani et al. (2015), Rajaselvam et al. (2012)
Klebsiella aerogenes	–	–	–	W	Samy et al. (1999)
Klebsiella pneumoniae	A, E	EA	H	C, M	Devi and Raj (2013), Govindarajan et al. (2008b), Pragada et al. (2011), Saranraj et al. (2010), Soruba et al. (2015)
Proteus mirabilis	–	EA, M, A	H, PE, C	–	Pragada et al. (2011), Selvamani and Balamurugan (2015a), Soruba et al. (2015)
Proteus vulgaris	–	–	C, EA, M, PE, A	H	Govindarajan et al. (2008b), Selvamani and Balamurugan (2015a)
Pseudomonas species	–	–	M	W	Manonmani et al. (2015)
Pseudomonas aeruginosa	–	H, E, M, C, EA, PE, DE, W	A	–	Baharum (2015), Divya et al. (2014), Govindarajan et al. (2008b), Hussain and Kumaresan (2013); Mohan et al. (2012), Muthuvelan and Raja (2008), Pragada et al. (2011), Ruslan (2015), Samy et al. (1999), Saranraj et al. (2010), Selvamani and Balamurugan (2015a)
Salmonella species	A, E, M	–	–	W	Devi and Raj (2013), Manonmani et al. (2015), Noriko (2013)
Salmonella enterica	M	–	–	–	Soruba et al. (2015)
Salmonella enteritidis	–	–	E, W	C	Somchit et al. (2010)
Salmonella typhi	M, E	EA	–	–	Hussain and Kumaresan (2013), Mohan et al. (2012), Saranraj et al. (2010)
Salmonella typhimurium	–	H, EA, M	–	–	Pragada et al. (2011)
Shigella flexneri	E	EA, A	PE, C, M		Saranraj et al. (2010), Selvamani and Balamurugan (2015a)
Vibrio cholerae	–	E	EA	–	Saranraj et al. (2010)
Vibrio damsela	–	–	–	W	Samy et al. (1999)

A = Acetone; C = Chloroform; E = Ethanol; EA = Ethyl acetate; DE = Diethyl ether; H = Hexane; M = Methanol; PE = Petroleum ether; W = Water.

lated with chitosan-casein. Similar phytochemical content in methanolic and ethanolic extracts has led to both extracts having anti-cancer properties. These results indicate that *Acalypha indica* can be implemented as a natural anti-cancer drug for certain cancer types.

5.2.6. Anti-diabetic

Further, *Acalypha indica* has potential as an anti-diabetic activity when the whole plant is used in the treatment. The phytochemicals from hexane, petroleum ether, chloroform, acetone and a mixture of methanol and acetone extracts showed some significant activities on the related assays and in vivo tests as shown in Table 10. Nandhakumar et al. (2009) indicated the hexane and chloroform extract inhibited alpha amylase activity up to 84.51% and 75.32%, respectively. Amylase is an enzyme that catalyzes and hydrolyses starch into sugar. If sugar levels elevate, this can lead to diabetic problems in humans. A continuity of the study has been carried out by Saha and Ahmed (2011a, 2011b) and Masih et al. (2011) through in vivo tests on rats. Both of them used the diabetes induction method on rats before the plant extract was introduced via oral The blood sugar levels decreased at least 25% after the administration of plant extract, followed by decreases in levels of cholesterol, urea and triglycerides levels after five hours. The streptozotocin was used to cause a rapid destruction of pancreatic β cells which led to impaired glucose-stimulated insulin release and resistance. These are the marker features for type II diabetes studies in rats. The ability of plant extract to inhibit the destruction of pancreatic β cells will determine whether the herb is useful or not. In this case, the whole of *Acalypha indica* can be used as an herb for anti-diabetic activity. This data supports the application of *Acalypha indica* as an agent to lower blood sugar by some people in India (Chopra et al., 1956). In their practice, the root alone is used to treat high blood sugar levels whereas, in the studies, the whole plant has proven to be more effective. This is possibly due to the root containing small amounts of cyanogenic phytochemical compared to the aerial part (Hungeling et al., 2009).

5.2.7. Anti-fungal

Eight kinds of fungi (*Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Candida albican, Candida glabrata, Candida tropicalis, Microsporum canis and Penicillium chrysogenum*) have been used to test whether *Acalypha indica* has an anti-fungal activity or not; these tests were conducted by Selvamani and Balamurugan (2015a, 2015b), Sakhti et al. (2011), Solomon et al. (2005) and Somchit et al. (2010). Nine solvents were used including hexane, petroleum ether, diethyl ether, chloroform, ethyl acetate, acetone, methanol, ethanol and water to extract the compounds inside *Acalypha indica*. The complete information on the anti-fungal activity of *Acalypha indica* is shown in Table 9. The similar approach for anti-bacterial classification is implemented to categorize the anti-fungal activity of *Acalypha indica*. As a general conclusion, there is still little information on anti-fungal activity from this plant except those which are currently available (Sakthi et al., 2011; Selvamani and Balamurugan, 2015a; Solomon et al., 2005; Somchit et al., 2010). The flavonoids inside *Acalypha indica* are expected to be the source of anti-fungal activity based on the other studies (Hnatyszyn et al., 2007). For anti-fungal activity, extraction from water like a decoction is not recommended since no fungi are affected by any phytochemicals inside. Raw use of the whole plant is suggested to treat fungal infections on the human body.

5.2.8. Anti-hyperlipidemic

Acalypha indica has anti-hyperlipidemic activity, as proven by Rajasekaran et al. (2013), on rats fed through an atherogenic induced diet. In this case, aqueous and ethanolic extracts from *Acalypha indica* leaves were administered into rats with 200 and 400 mg/kg/day doses for ten days. Simvastatin was used as a standard reference for this test with 10 mg/kg/day. The results showed that the anti-hyperlipidemic

Table 9
Summary of fungal inhibition activity by *Acalypha indica* extracts based on solvents used.

Fungi	Very active	Active	Weak	Inactive	Refs.
Aspergillus flavus	E	EA	–	–	Sakthi et al. (2011), Selvamani and Balamurugan (2015a)
Aspergillus fumigatus	EA	–	C, E	H, PE, DE, A, M, W	Sakthi et al. (2011), Somchit et al. (2010)
Aspergillus niger	A, C, H, M	–	–	EA, E	Sakthi et al. (2011), Solomon et al. (2005)
Candida albican	A, H, M	C, EA	E	W	Sakthi et al. (2011), Selvamani and Balamurugan (2015a), Solomon et al. (2005), Somchit et al. (2010)
Candida glabrata	–	–	E	EA	Sakthi et al. (2011)
Candida tropicalis	–	–	C	E, W	Selvamani and Balamurugan (2015a), Somchit et al. (2010)
Microsporum canis	–	C	E	W	Somchit et al. (2010)
Penicillium chrysogenum	–	–	E, EA	–	Sakthi et al. (2011)

A = Acetone; C = Chloroform; E = Ethanol; EA = Ethyl acetate; DE = Diethyl ether; H = Hexane; M = Methanol; PE = Petroleum ether; W = Water.

activity was optimum when the atherogenic induced diet and 400 mg ethanolic extract were incorporated together. Under those circumstances, the HDL value increased up to 51.80% while the LDL, VLDL, TC and TG values decreased to 42.48%, 24.38%, 30.00% and 24.29%, respectively. For the atherogenic induced diet and standard (Simvastatin), the HDL value increased to 70.01%, whereas the LDL, VLDL, TC and TG values decreased to 61.64%, 34.16%, 43.64% and 34.71%, respectively. Based on the results, *Acalypha indica* exhibited moderate anti-hyperlipidemic activity compared to the simvastatin. Indeed, the concentration of responsible phytochemicals inside the extract might be lower than the standard. According to Rajasekaran et al. (2013), the flavonoid and polyphenol from the extract were favorably considered in increasing HDL and decreasing LDL and VLDL. The diet contained cholesterol, cholic acid, peanut oil, sucrose and normal laboratory diet to induce the lipid on the rats. Any effort to find a treatment for hyperlipidemia is very much appreciated due to the increasing number of heart disease patients. Moreover, hyperlipidemia is a well-known factor related to cardiovascular disease (Nelson, 2013). In conclusion, water and ethanolic extracts from the aerial part of *Acalypha indica* can be used as anti-hyperlipidemic agents. Food high in cholesterol and raw *Acalypha indica* leaves should be eaten together when a patient has a problem with any related cardiovascular disease.

5.2.9. Anti-inflammatory

At the right dosage, *Acalypha indica* can behave as an anti-inflammatory medicine in the human body. Rahman et al. (2010) justified this activity of the *Acalypha indica* in the long evan rats by using methanolic extract. They used the anti-inflammation method (Winter et al., 1962) with minor modifications and selected phenylbutazone as the standard drug. The anti-inflammation effects were comparable with the standard until four hours after the injection of the carrageenan solution (Rahman et al., 2010). The anti-inflammation activities from methanolic extracts are also supported by Soruba et al. (2015), which resulted in the inhibition of albumin denaturation and proteinase. Both assays showed 80% of inhibition, indicating no protein denaturation when the extract was used. Protein denaturation is one of the indicators for inflammation activity in the human body. Muzammil et al. (2015) also mentioned the anti-inflammatory properties of this plant through the Human Red Blood Cell (HRBC) membrane stabilization method. They used the drug diclofenac as a standard control similar to analgesic activity. The plant extract stabilized the membrane by inhibiting hypotonicity-induced lysis of an erythrocyte membrane, analogous to a lysosomal membrane. The unstable lysosomal membrane contributed to the inflammatory response by releasing lysosomal constituents from activated neutrophil which further caused tissue inflammation. In a nutshell, these in vitro and in vivo tests demonstrate the capability of methanolic extract from the whole plant to reduce inflammation. Raw consumption is recommended for anti-inflammation treatment as well as analgesic and anti-arthritics. Several diseases such as rheumatoid arthritis, wound healing and skin irritation can be treated by using this plant as traditionally practiced by Asians especially in India and Nepal..

5.2.10. Anti-obesity

There are two types of experiments done to study the anti-obesity of *Acalypha indica* (Rajasekaran et al., 2013; Sathya et al., 2012). Sathya et al. (2012) conducted a study using various concentrations of ethanolic extract through a weight assessment for 28 days on Albino wistar rats. They claimed there was no significant increment in rat weight during the experiment. Rajasekaran et al. (2013) furthered the study by using a high-fat content diet together with ethanolic extract on Albino wistar rats. The mean body weight of the rats on the tenth day was measured to compare between the standard (Simvastatin) and the 400 mg ethanolic extract. Both groups increased by 24.14% and 24.61% after being fed the atherogenic induced diet, while the group of rats who were only fed the atherogenic induced diet had a high value of mean body weight percentage (29.56%). The ethanolic extract exhibited similar results to the standard drug used in the experiment. The flavonoid inside *Acalypha indica* like quercetin also played a role as a potential anti-obesity drug (Moon et al., 2013).

5.2.11. Antioxidant

There are three types of assays used for antioxidant measurement as shown in Table 10. The 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), 2,2-diphenylpicrylhydrazyl (DPPH) and Xanthine oxidase assays are used to test antioxidant activities from various *Acalypha indica* extracts from a certain plant part. As a result, these antioxidant studies are quite inconsistence and dubious. For example, the hexane extract results showed the antioxidant value from zero to very strong activities (Muthuvelan and Raja, 2008; Pragada et al., 2011; Ruslan, 2015; Sanseera et al., 2012). The presented results in this review are influenced by how the researchers prepared the sample and where the sample came from. The data is unreliable but still significant as a reference for future study. According to Table 10, the whole plant has antioxidant activities, especially the phytochemicals from semi-polar and polar groups. More studies are needed to improve the antioxidant activity results from non-polar phytochemicals. To date, no study has related to the antioxidant activity of *Acalypha indica* essential oil that might be very useful for therapeutic activities as discussed in Section 4.2. Antioxidant phytochemicals play major roles in treating some diseases such as rheumatoid arthritis, diarrhea, wound healing, and others as practiced by most people in Table 3.

5.2.12. Anti-tubercular

Tuberculosis is a disease caused by bacterial infection, particularly to the lung and could lead to death if not treated properly. Tuberculosis is one of the top ten causes of death in the world (World Health Organization, 2017). Research treatment related to this disease is highly recommended for saving more lives, especially with low-cost medication. Since *Acalypha indica* has been used by people in India to treat any disease related to the breathing system (Jayaprakasam and

Table 10
Summary of pharmacological activities of the extracts from different parts of *Acalypha indica*.

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
Analgesic	MeOH	5.1	WP	Writhing reflex method	Showed writhing inhibition activity with a 57.2% increment at 400 mg/kg dosage on mice	Rahman et al. (2010)
Anthelmintic activity	EtOH	5.1	AP	Anthelmintic assay	Showed paralysis activity 10 min after application and death after 29 min at 100 mg/ml on Pp	Ranju et al. (2011)
	EtOH	5.1	R	Anthelmintic assay	Showed paralysis activity 20 min after application and death after 30 min at 50 mg/ml on Pp	Chengaiah et al. (2009)
	Water	9.0	AP	Anthelmintic assay	Showed paralysis activity 12 min after application and death after 32 min at 100 mg/ml on Pp	Ranju et al. (2011)
Anti-arthritics	MeOH	5.1	L	Proteinase inhibition assay	0.1 mg/ml of extract exhibited a 80% increment of proteinase inhibition activity	Soruba et al. (2015)
	MeOH	5.1	R	Proteinase inhibitory assay	Showed proteinase inhibitory activity with IC_{50} value of 0.037 mg/ml	Jayaprakasam and Ravi (2013)
	MeOH	5.1	L	Inhibition of albumin denaturation assay	0.1 mg/ml of extract exhibited a 80% increment of albumin denaturation inhibition activity	Soruba et al. (2015)
	MeOH	5.1	R	Inhibition of protein denaturation	Showed inhibition of protein denaturation activity with IC_{50} value of 0.052 mg/ml	Jayaprakasam and Ravi (2013
	MeOH	5.1	R	Anti-hyaluronidase activity	Showed hyaluronidase enzymes inhibition with IC_{50} value of 0.018 mg/ml	Jayaprakasam and Ravi (2013)
Anti-bacterial	Hexane	0.0	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	Hexane	0.0	AP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	Hexane	0.0	R	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	Hexane	0.0	Stem	Disc diffusion method	Showed inhibition activity against Ec 119% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	L	Disc diffusion method	Showed inhibition activity against Ec 119% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	R	Disc diffusion method	Showed inhibition activity against Ec 95% better than blank at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	L	Microdilution method	Active with MIC and MBC value of 0.5 mg/ml against Rm	Batubara et al. (2016)
	Hexane	0.0	L	Biofilm degradation method	Active with IC_{50} value of 0.197 mg/ml against Rm	Batubara et al. (2016)
	Hexane	0.0	L	MIC	Active with MIC value of 0.312 mg/ml against Sa, Se (1.25 mg/ml), Bc (0.312 mg/ml), Rf (0.156 mg/ml) and Pa (5 mg/ml)	Govindarajan et al. (2008b)
	Hexane	0.0	L	MIC	Inactive against Kp, Ec and Tv at a concentration of 10 mg/ml	Govindarajan et al. (2008b)
	Hexane	0.0	L	MMC	Active with MMC value of 0.625 mg/ml against Sa, Se (5 mg/ml), Bc (0.625 mg/ml), Rf (0.312 mg/ml) and Pa (10 mg/ml)	Govindarajan et al. (2008b)
	Hexane	0.0	L	MMC	Inactive against Kp, Ec and Tv at a concentration of 10 mg/ml	Govindarajan et al. (2008b)
	Hexane	0.0	L	Disc diffusion method	Showed inhibition activity against Sa, Se, Bc, Rf and Pa at a concentration of 5 mg/disc	Govindarajan et al. (2008b)
	Hexane	0.0	L	Disc diffusion method	Inactive against Kp, Ec and Tv on 10 mg/ml	Govindarajan et al. (2008b)
	Hexane	0.0	WP	Cup plate method	Showed inhibition activity against Bm, Se, Pa, Tm, KpMm, Ea, Ec and El at a concentration of 50 mg/ml	Pragada et al. (2011)
	Hexane	0.0	AP	Well diffusion method	Showed inhibition activity against Ah and Sa at a volume of 0.1 ml	Muthuvelan and Raja (2008)
	Hexane	0.0	AP	Well diffusion method	Inactive against Ec, Pa, Ry and Bc at a volume of 0.1 ml	Muthuvelan and Raja (2008)
	PE	0.1	Unstated	Disc diffusion method	Showed inhibition activity against Sa, Ry, Ec, Pa, Tv, Hf and Tm at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	DE	2.8	AP	Well diffusion method	Showed inhibition activity against Ec, Ah and Sa at a volume of 0.1 ml	Muthuvelan and Raja (2008)
	DE	2.8	AP	Well diffusion method	Inactive against Pa, Rp and Bc	Muthuvelan and Raja (2008)
	Chloroform	4.1	AP	Well diffusion method	Showed inhibition activity against Ah at a volume of 0.1 ml	Muthuvelan and Raja (2008)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
	Chloroform	4.1	AP	Well diffusion method	Inactive against Pa, Rp and Bc	Muthuvelan and Raja (2008)
	Chloroform	4.1	Stem	Disc diffusion method	Showed inhibition activity against Ec 104% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	L	Disc diffusion method	Showed inhibition activity against Ec 76% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	R	Disc diffusion method	Showed inhibition activity against Ec 104% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	L	Biofilm degradation method	Active with IC_{50} value of 0.149 mg/ml against Rm	Batubara et al. (2016)
	Chloroform	4.1	L	Microdilution method	Inactive against Rm	Batubara et al. (2016)
	Chloroform	4.1	L	Disc diffusion method	Showed inhibition activity against Sa, Se, Bc, Rf and Pa at a concentration of 5 mg/disc	Govindarajan et al. (2008b)
	Chloroform	4.1	L	Disc diffusion method	Inactive against Kp, Ec and Tv at a concentration of 5 mg/disc	Govindarajan et al. (2008b)
	Chloroform	4.1	L	MIC	Active with MIC value of 0.625 mg/ml against Sa, Se (1.25 mg/ml), Bc (0.625 mg/ml), Rf (0.312 mg/ml) and Pa (2.5 mg/ml)	Govindarajan et al. (2008b)
	Chloroform	4.1	L	MIC	Inactive against Kp, Ec and Tv at a concentration of 5 mg/ml	Govindarajan et al. (2008b)
	Chloroform	4.1	L	MMC	Active with MMC value of 1.25 mg/ml against Sa, Se (5 mg/ml), Bc (1.25 mg/ml), Rf (0.625 mg/ml) and Pa (5 mg/ml)	Govindarajan et al. (2008b)
	Chloroform	4.1	L	MMC	Inactive against Kp, Ec and Tv at a concentration of 5 mg/ml	Govindarajan et al. (2008b)
	Chloroform	4.1	Unstated	Disc diffusion method	Showed inhibition activity against Sa, Ry; Ec, Pa, Tv, Hf and Tm at concentration 1 mg/ml	Selvamani and Balamurugan (2015a)
	Chloroform	4.1	AP	Disc diffusion method	Inactive against Ec, Md, Sa and Bs at a concentration 30 mg/ml	Somchit et al. (2010)
	EA	4.4	L	Disc diffusion method	Showed inhibition activity against Sa, Se, Bc, Rf and Pa at a concentration of 5 mg/disc	Govindarajan et al. (2008b)
	EA	4.4	L	Disc diffusion method	Inactive against Kp, Ec and Tv at a concentration of 10 mg/ml	Govindarajan et al. (2008b)
	EA	4.4	L	MIC	Active with MIC value of 0.312 mg/ml against Sa, Se (1.25 mg/ml), Bc (0.625 mg/ml), Rf (0.312 mg/ml) and Pa (5 mg/ml)	Govindarajan et al. (2008b)
	EA	4.4	L	MIC	Inactive against Kp, Ec and Tv at a concentration of 10 mg/ml	Govindarajan et al. (2008b)
	EA	4.4	L	MMC	Active with MMC value of 0.625 mg/ml against Sa, Se (5 mg/ml), Bc (1.25 mg/ml), Rf (0.625 mg/ml) and Pa (10 mg/ml)	Govindarajan et al. (2008b)
	EA	4.4	L	MMC	Inactive against Kp, Ec and Tv at a concentration of 10 mg/ml	Govindarajan et al. (2008b)
	EA	4.4	WP	Cup plate method	Showed inhibition activity against Bm, Se, Pa, Tm, KpMm, Ea, Ec and El at a concentration of 50 mg/ml	Pragada et al. (2011)
	EA	4.4	L	Well diffusion method	Showed inhibition activity against Sa, Bs, Bc, Ec, Mp, Hf, Kp and Vc at 100 mg weight	Saranraj et al. (2010)
	EA	4.4	L	Well diffusion method	Inactive against Pa at 100 mg weight	Saranraj et al. (2010)
	EA	4.4	Unstated	Disc diffusion method	Showed inhibition activity against Sa, Ry, Ec, Pa, Tv, Hf and Tm at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	Acetone	5.1	Stem	Disc diffusion method	Showed inhibition activity against Ec with 85% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	L	Disc diffusion method	Showed inhibition activity against Ec with 71% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	R	Disc diffusion method	Showed inhibition activity against Ec with 66% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	Stem	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 µl	Devi and Raj (2013)
	Acetone	5.1	L	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp and Kp at a volume of 100 µl	Devi and Raj (2013)
	Acetone	5.1	L	Well diffusion method	Inactive against Pa at a volume of 100 µl	Devi and Raj (2013)
	Acetone	5.1	R	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 µl	Devi and Raj (2013)
	Acetone	5.1	Unstated	Disc diffusion method	Showed inhibition activity against Sa, Ry, Ec, Pa, Tv, Hf and Tm at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	Acetone	5.1	AP	Well diffusion method	Showed inhibition activity against Ec, Sa, Ksp and Bs at a volume of 100 µl	Rajaselvam et al. (2012)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
	Acetone	5.1	AP	Disc diffusion method	Showed inhibition activity against Sa and Pa at a volume of 5 μl	Divya et al. (2014)
	Acetone	5.1	AP	Well diffusion method	Showed inhibition activity against Sa and Pa at a volume of 5 μl	Divya et al. (2014)
	EtOH	5.1	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	EtOH	5.1	AP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	EtOH	5.1	R	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	EtOH	5.1	Stem	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 μl	Devi and Raj (2013)
	EtOH	5.1	L	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 μl	Devi and Raj (2013)
	EtOH	5.1	R	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 μl	Devi and Raj (2013)
	EtOH	5.1	L	Well diffusion method	Showed inhibition activity against Sa, Bs, Bc, Ec, Mp, Hf, Kpe, Vc and Pa at 100 mg weight	Saranraj et al. (2010)
	EtOH	5.1	AP	Unstated	Showed inhibition activity against Ec, Mp and Pa at a concentration of 0.05 mg/ml	Mohan et al. (2012)
	EtOH	5.1	AP	Unstated	Inactive against Sa at 0.05 mg/ml	Mohan et al. (2012)
	EtOH	5.1	AP	Disc diffusion method	Showed inhibition activity against Ec, Md, Sa and Bs at a concentration of 30 mg/ml	Somchit et al. (2010)
	MeOH	5.1	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	MeOH	5.1	AP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	MeOH	5.1	AP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Ruslan (2015)
	MeOH	5.1	L	Disc diffusion method	Showed inhibition activity against Bsp, Ec, Msp, Ksp and Psp at a volume of 100 μl	Manonmani et al. (2015)
	MeOH	5.1	L	Disc diffusion method	Inactive against Ssp at a volume of 100 μl	Manonmani et al. (2015)
	MeOH	5.1	Unstated	Disc diffusion method	Showed inhibition activity against Sa, Ry, Ec, Pa, Tv, Hf and Tm at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	MeOH	5.1	WP	Cup plate method	Showed inhibition activity against Bm, Se, Pa, Tm, Kp, Mm, Ea, Ec and El at a concentration of 50 mg/ml	Pragada et al. (2011)
	MeOH	5.1	Stem	Disc diffusion method	Showed inhibition activity against Ec with 95% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	L	Disc diffusion method	Showed inhibition activity against Ec with 109% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	R	Disc diffusion method	Showed inhibition activity against Ec with 119% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	L	Microdilution method	Active with MIC value of 0.5 mg/ml against Rm	Batubara et al. (2016)
	MeOH	5.1	L	Microdilution method	Inactive with MBC value of 0.5 mg/ml against Rm	Batubara et al. (2016)
	MeOH	5.1	L	Biofilm degradation method	Active with IC_{50} value of 0.214 mg/ml against Rm	Batubara et al. (2016)
	MeOH	5.1	Stem	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp. at a volume of 100 μl	Devi and Raj (2013)
	MeOH	5.1	L	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 μl	Devi and Raj (2013)
	MeOH	5.1	R	Well diffusion method	Showed inhibition activity against Ssp, Ec, Msp, Kp and Psp at a volume of 100 μl	Devi and Raj (2013)
	MeOH	5.1	L	Disc diffusion method	Showed inhibition activity against Sa, Se, Bc, Rf and Pa at a concentration of 5 mg/disc	Govindarajan et al. (2008b)
	MeOH	5.1	L	Disc diffusion method	Inactive against Kpe, Ec and Tv at a concentration of 5 mg/ml	Govindarajan et al. (2008b)
	MeOH	5.1	L	MIC	Active with MIC value of 0.156 mg/ml against Sa, Se (0.625 mg/ml), Bc (0.156 mg/ml), Rf (0.156 mg/ml) and Pa (2.5 mg/ml)	Govindarajan et al. (2008b)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
	MeOH	5.1	L	MIC	Inactive against Kp, Ec and Tv at a concentration of 5 mg/ml	Govindarajan et al. (2008b)
	MeOH	5.1	L	MMC	Active with MMC value of 0.312 mg/ml against Sa, Se (1.25 mg/ml), Bc (0.312 mg/ml), Rf (0.312 mg/ml) and Pa (5 mg/ml)	Govindarajan et al. (2008b)
	MeOH	5.1	L	MMC	Inactive against Kp, Ec and Tv at a concentration of 5 mg/ml	Govindarajan et al. (2008b)
	MeOH	5.1	L	Unstated	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 50 μg/ml	Hussain and Kumaresan (2013)
	MeOH	5.1	L	Well diffusion method	Showed inhibition activity against Kp, Sa, Tm, Ec, La and Mt at a volume of 0.02 ml	Soruba et al. (2015)
	MeOH	5.1	L	MIC	Active with MIC value of 0.007 mg/ml against Kp, Mt (0.017 mg/ml) Ec (0.002 mg/ml) and La (0.031 mg/ml)	Soruba et al. (2015)
	Water	9.0	WP	Disc diffusion method	Inactive activity against Ec, Mp, Pa and Sa at a concentration of 0.5 mg/ml	Baharum (2015)
	Water	9.0	AP	Disc diffusion method	Inactive activity against Ec, Mp, Pa and Sa at a concentration of 0.5 mg/ml	Baharum (2015)
	Water	9.0	R	Disc diffusion method	Inactive activity against Ec, Mp, Pa and Sa at a concentration of 0.5 mg/ml	Baharum (2015)
	Water	9.0	AP	Disc diffusion method	Showed inhibition activity against Ah (30 and 40 mg) and Pa (40 mg) after 24 h at 37 °C incubation	Samy et al. (1999)
	Water	9.0	AP	Disc diffusion method	Inactive against Av, Ec, Ka, Vd, Bc, Ry and Csp (40 mg) after 24 h at 37 °C incubation	Samy et al. (1999)
	Water	9.0	AP	Disc diffusion method	Showed inhibition activity against Ah (30 and 40 mg) and Bc (40 mg) after 48 h at 37 °C incubation	Samy et al. (1999)
	Water	9.0	AP	Disc diffusion method	Inactive against Av, Ec, Ka, Pa, Vd, Ry and Csp (40 mg) after 48 h at 37 °C incubation	Samy et al. (1999)
	Water	9.0	L	Disc diffusion method	Showed inhibition activity against Bsp and Ec at a volume of 0.1 ml	Manonmani et al. (2015)
	Water	9.0	L	Disc diffusion method	Inactive against Msp, Ksp and Psp at a volume of 0.1 ml	Manonmani et al. (2015)
	Water	9.0	AP	Disc diffusion method Well diffusion method	Showed inhibition activity against Sa and Pa at a volume of 5 μl	Divya et al. (2014)
	Water	9.0	AP	Well diffusion method	Showed inhibition activity against Ec, Sa and Bs at a volume of 100 μl	Rajaselvam et al. (2012)
	Water	9.0	AP	Well diffusion method	Inactive against Ksp at a volume of 0.1 ml	Rajaselvam et al. (2012)
	Water	9.0	AP	Disc diffusion method	Showed inhibition activity against Ec, Md, Sa and Bs at a concentration of 30 ml/ml	Somchit et al. (2010)
	Water	9.0	L	Disc diffusion method	Showed inhibition activity against Mp at certain volume	Noriko (2013)
	50 Water: 50 Acetic acid	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	50 Water: 50 Acetic acid	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	50 Water: 50 Acetic acid	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	50 Water: 50 EtOH	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	50 Water: 50 EtOH	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	50 Water: 50 EtOH	–	WP	Disc diffusion method	Showed inhibition activity against Ec, Mp, Pa and Sa at a concentration of 60 mg/ml	Baharum (2015)
	70% alcohol	–	WP	Cup plate method	Showed inhibit activity against Bm, Se, Pa, Tm, Kp, Mm, Ea, Ec and El at a concentration of 50 mg/ml	Pragada et al. (2011)
Anti-cancer	EtOH	5.1	AP	MTT assay	Encapsulation with chitosan-casein increases the effect on human prostate cell line PC3 after 72 h incubation	Amarnath et al. (2014)
	MeOH	5.1	AP	Resazurin Microplate assay	Showed high inhibition activity with IC_{50} of 0.025 mg/ml against NCI-H187 Small Cell Lung Cancer	Sanseera et al. (2012)
	MeOH	5.1	AP	Resazurin Microplate assay	Inactive against KB-oral cavity cancer	Sanseera et al. (2012)
	MeOH	5.1	AP	Resazurin Microplate assay	Inactive against MCF7-breast cancer	Sanseera et al. (2012)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
Anti-cholesterol	70 MeOH: 30 Acetone	–	WP	Induction of diabetes test	Cholesterol level decreased 33% after 5 h administration with 300 mg/kg on AWR.	Masih et al. (2011)
	70 MeOH: 30 Acetone	–	WP	Induction of diabetes test	Triglyceride level decreased 7% after 5 h administration with 300 mg/kg on AWR.	Masih et al. (2011)
Anti-diabetic	Hexane	0.0	Unstated	Porcine pancreatic amylase inhibitory assay	Showed inhibition activity against alpha-amylase 84.51% better than blank at a concentration of 0.1 mg/ml	Nandhakumar et al. (2009)
	PE	0.1	Whole part	Streptozotocin induced diabetic	100 mg/kg of extract reduced 43% of blood sugar level of fasting rat	Saha and Ahmed (2011a)
	Chloroform	4.1	Unstated	Porcine pancreatic amylase inhibitory assay	Showed inhibition activity against alpha-amylase of 75.32% better than blank at a concentration of 0.1 mg/ml	Nandhakumar et al. (2009)
	Chloroform	4.1	Whole part	Streptozotocin induced diabetic	100 mg/kg of extract reduced 45% of blood sugar level of fasting rat	Saha and Ahmed (2011a)
	Acetone	5.1	Whole part	Streptozotocin induced diabetic	100 mg/kg of extract reduced 48% blood sugar level of fasting rat	Saha and Ahmed (2011a)
	MeOH	5.1	Whole part	Streptozotocin induced diabetic	100 mg/kg of extract reduced 51% of blood sugar level of fasting rat	Saha and Ahmed (2011a)
	70 MeOH: 30 Acetone	–	WP	Glucose tolerance test	Glucose level decreased after 60 min administration with extract 300 mg/kg in the AWR.	Masih et al. (2011)
					Glucose level decreased 25% after 5 h administration with extract 300 mg/kg in the AWR.	Masih et al. (2011)
	70 MeOH: 30 Acetone	–	WP	Induction of diabetes test	Urea level decreased 23% after 5 h administration with 300 mg/kg in the AWR.	Masih et al. (2011)
Anti-fungal	Hexane	0.0	R	Disc diffusion method	Showed inhibition activity against An with 71% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	Stem	Disc diffusion method	Showed inhibition activity against An with 61% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	L	Disc diffusion method	Showed inhibition activity against An with 85% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	Stem	Disc diffusion method	Showed inhibition activity against Ca with 90% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	L	Disc diffusion method	Showed inhibition activity against Ca with 95% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Hexane	0.0	R	Disc diffusion method	Showed inhibition activity against Ca with 76% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	PE	0.1	Unstated	Disc diffusion method	Showed inhibition activity against Ca, Ct and Al at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	Chloroform	4.1	Unstated	Disc diffusion method	Showed inhibition activity against Ca, Ct and Al at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	Chloroform	4.1	AP	Disc diffusion method	Inactive against Ca and Mc at a concentration of 30 mg/ml	Somchit et al. (2010)
	Chloroform	4.1	R	Disc diffusion method	Showed inhibition activity against An with 61% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	Stem	Disc diffusion method	Showed inhibition activity against An with 71% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	L	Disc diffusion method	Showed inhibition activity against An with 104% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	R	Disc diffusion method	Showed inhibition activity against Ca with 85% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	Stem	Disc diffusion method	Showed inhibition activity against Ca with 85% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Chloroform	4.1	L	Disc diffusion method	Showed inhibition activity against Ca with 95% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	EA	4.4	Unstated	Disc diffusion method	Showed inhibition activity against Ca, Ct and Al at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	EA	4.4	L	Well diffusion method	Showed inhibition activity against Ca, Am, Al and Pc at a concentration of 300 mg/ml	Sakthi et al. (2011)
	Acetone	5.1	Unstated	Disc diffusion method	Showed inhibition activity against Ca, Ct and Al at a concentration of	Selvamani and Balamurugan

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
					1 mg/ml	(2015a)
	Acetone	5.1	R	Disc diffusion method	Showed inhibition activity against An with 52% viability at a concentration with 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	Stem	Disc diffusion method	Showed inhibition activity against An with 71% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	L	Disc diffusion method	Showed inhibition activity against An with 71% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	R	Disc diffusion method	Showed inhibition activity against Ca with 66% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	Stem	Disc diffusion method	Showed inhibition activity against Ca with 95% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Acetone	5.1	L	Disc diffusion method	Showed inhibition activity against Ca with 61% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	EtOH	5.1	L	Well diffusion method	Showed inhibition activity against Ca, Cg, Am, Al and Pc at a concentration of 300 mg/ml	Sakthi et al. (2011)
	EtOH	5.1	AP	Disc diffusion method	Showed inhibition activity against Ca, Ct, Mc and Am	Somchit et al. (2010)
	MeOH	5.1	Unstated	Disc diffusion method	Showed inhibition activity against Cas, Ct and Al at a concentration of 1 mg/ml	Selvamani and Balamurugan (2015a)
	MeOH	5.1	R	Disc diffusion method	Showed inhibition activity against An with 57% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	Stem	Disc diffusion method	Showed inhibition activity against An with 85% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	L	Disc diffusion method	Showed inhibition activity against An with 66% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	R	Disc diffusion method	Showed inhibition activity against Ca with 109% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	Stem	Disc diffusion method	Showed inhibition activity against Ca with 95% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	MeOH	5.1	L	Disc diffusion method	Showed inhibition activity against Ca with 119% viability at a concentration of 0.2 mg/ml	Solomon et al. (2005)
	Water	9.0	AP	Disc diffusion method	Inactive against Ca, Ct, Mc and Am	Somchit et al. (2010)
Anti-hyperlipidemic	EtOH	5.1	AP	Atherogenic diet induced	The 400 mg/kg extract dosage increased HDL (51.8%) and reduced LDL (42.48%), VLDL (24.38%) and TC (30.00%) on AWR	Rajasekaran et al. (2013)
	Water	9.0	AP	Atherogenic diet induced	400 mg/kg extract dosage increased HDL (43.97%) and reduced LDL (28.79%), VLDL (19.85%) and TC (20.01%) on AWR	Rajasekaran et al. (2013)
Anti-inflammatory	MeOH	5.1	WP	Carrageenan-induced in rat paw inflammation	Maximum inhibition increased 21.5% of 125 mg/kg and 30.6% of 250 mg/kg after 3 h	Rahman et al. (2010)
	MeOH	5.1	L	Inhibition of albumin denaturation assay	0.1 mg/ml of extract exhibited a 80% increment of albumin denaturation inhibition activity	Soruba et al. (2015)
	MeOH	5.1	L	Proteinase inhibition	0.1 mg/ml of extract exhibited a 80% increment of proteinase inhibition activity	Soruba et al. (2015)
	MeOH	5.1	L	HRBC membrane stabilization method	Showed inhibition activity of 78.72% at a concentration of 0.25 mg/ml	Muzammil et al. (2015)
Anti-larvicidal activity	Benzene	2.7	AP	WHO standard (Determination on insecticides)	Active with LC_{90} value of 41.29 ppm against As	Govindarajan et al. (2008a)
	Chloroform	4.1	AP	WHO standard (Determination on insecticides)	Active with LC_{90} value of 58.27 ppm against As	Govindarajan et al. (2008a)
	EA	4.4	AP	WHO standard (Determination on insecticides)	Active with LC_{90} value of 49.19 ppm against As	Govindarajan et al. (2008a)
	MeOH	5.1	AP	WHO standard (Determination on insecticides)	Active with LC_{90} value of 36.32 ppm against As	Govindarajan et al. (2008a)
	MeOH	5.1	AP	Larva and pupal assay	Active with LC_{50} value of 292.5 ppm against $instar_1$, $instar_2$ (327.9 ppm), $instar_3$ (365.3 ppm), $instar_4$ (420.6 ppm) and pupa (467.6 ppm) of Ae	Kamalakannan et al. (2011)
	MeOH	5.1	AP	Smoke toxicity assay	Mosquito coils containing extract (10 g/2.16 × 10^5 cm^3 per 24 h) killed 19.4% of blood fed Ae	Kamalakannan et al. (2011)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
Anti-obesityAntioxidant	EtOH	5.1	AP	Atherogenic Diet induced	400 mg/kg extract dosage exhibited 24.61% of body weight reduction on AWR	Rajasekaran et al. (2013)
	EtOH	5.1	Unstated	Weight assessment	500 mg/kg extract dosage did not show any significant weight difference until 28 days on AWR	Sathya et al. (2012)
	Water	9.0	AP	Atherogenic Diet induced	400 mg/kg extract dosage exhibited 22.05% of body weight reduction on AWR	Rajasekaran et al. (2013)
	Hexane	0.0	WP	DPPH assay	Exhibited activity with IC_{50} of 0.25 mg/ml	Pragada et al. (2011)
	Hexane	0.0	AP	DPPH assay	Exhibited activity with IC_{50} of 6.19 mg/ml	Sanseera et al. (2012)
	Hexane	0.0	AP	ABTS assay	Exhibited activity with IC_{50} of 6.13 mg/ml	Sanseera et al. (2012)
	Hexane	0.0	AP	DPPH assay	Exhibited 78.11% inhibition at a concentration of 0.1 mg/ml	Muthuvelan and Raja (2008)
	Hexane	0.0	WP	DPPH assay	No activity at a concentration of 0.5 mg/ml	Ruslan (2015)
	Chloroform	4.1	AP	ABTS assay	Exhibited activity with IC_{50} of 6.31 mg/ml	Sanseera et al. (2012)
	Chloroform	4.1	AP	DPPH assay	Exhibited activity with IC_{50} of 5.70 mg/ml	Sanseera et al. (2012)
	EA	4.4	WP	DPPH assay	Exhibited activity with IC_{50} of 0.2 mg/ml	Pragada et al. (2011)
	EtOH	5.1	WP	DPPH	Exhibited activity with IC_{50} of 0.461 mg/ml	Ruslan (2015)
	MeOH	5.1	WP	DPPH assay	Exhibited activity with IC_{50} of 0.4 mg/ml	Pragada et al. (2011)
	MeOH	5.1	WP	DPPH	Exhibited activity with IC_{50} of 0.334 mg/ml	Ruslan (2015)
	MeOH	5.1	AP	DPPH assay	Exhibited activity with IC_{50} of 7.79 mg/ml	Sanseera et al. (2012)
	MeOH	5.1	AP	ABTS assay	Exhibited activity with IC_{50} of 6.37 mg/ml	Sanseera et al. (2012)
	MeOH	5.1	L	Xanthine oxidase assay	No activity at a concentration of 0.1 mg/ml	Umamaheswari et al. (2007)
	Water	9.0	WP	DPPH	Exhibited activity with IC_{50} of 0.111 mg/ml	Baharum (2015)
	Water	9.0	L	Xanthine oxidase assay	No activity at concentration 0.1 mg/ml	Umamaheswari et al. (2007)
	70 Water: 30 EtOH	–	AP	DPPH assay	Exhibited activity with IC50 of 0.062 mg/ml	Ibrahim (2016)
	70 Water: 30 EtOH	–	R	DPPH assay	Exhibited activity with IC50 of 0.206 mg/ml	Ibrahim (2016)
	50 Water: 50 EtOH	–	WP	DPPH	Exhibited activity with IC_{50} of 0.125 mg/ml	Baharum (2015)
	50 Water: 50 Acetic acid	–	WP	DPPH	Exhibited activity with IC_{50} of 0.105 mg/ml	Baharum (2015)
	50 Water: 50 MeOH	–	L	Xanthine oxidase assay	No activity at a concentration of 0.1 mg/ml	Umamaheswari et al. (2007)
	70% alcohol	–	WP	DPPH assay	Exhibited activity with IC_{50} of 0.4 mg/ml	Pragada et al. (2011)
Anti-tubercular	EtOH	5.1	L	MIC	Inactive against M. tuberculosis H37Rv, H-485, SH-577 and SHOF-567 at a concentration of 0.5 mg/ml	Chidambaram and Swaminathan (2013)
	Water	9.0	L	Colony forming units	4% v/v of extract inhibited 68% of M. tuberculosis H37Rv, DKU-156 (95%) and JAL-1236 (68%). Inactive against M. fortuitum TMC-1529	Gupta et al. (2010)
	Water	9.0	L	MIC	Inactive against M. tuberculosis H37Rv, H-485, SH-577 and SHOF-567	Chidambaram and Swaminathan (2013)
Anti-ulcer	MeOH	5.1	WP	Pylorus ligation method	200 mg/kg extract dosage showed no signs of redness and inflammation, reduction of volume of gastric juice (77.14%), increment in pH value to 4 compared to negative control 1.3, reduction of total acidity (69.29%), reduction of free acidity (63.24%) and reduction of ulcer index (47.18%) in AR	Kalimuthu et al. (2010)
	MeOH	5.1	WP	Swim stress induced ulceration	200 mg/kg extract dosage showed no sign of redness, inflammation and reduction of ulcer index (41.46%) in AR	Kalimuthu et al. (2010)
Anti-urolithiasis	EtOH	5.1	Unstated	Ethylene glycol induced urolithiasis	200 mg/kg extract dosage significantly reduced Ca^{2+} ATPase, Mg^{2+} ATPase, Na^{+} K^{+} ATPase activity in liver and kidney of AWR	Sathya et al. (2011)
Anti-venom	PE	0.1	L	Neutralization lethal venom method	500 mg/kg extract dosage increased the survival rate of 25% in SAM	Rajendran et al. (2010)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
	Benzene	2.7	L	Neutralization lethal venom method	500 mg/kg extract dosage increased the survival rate of 37% in SAM	Rajendran et al. (2010)
	Chloroform	4.4	L	Neutralization lethal venom method	500 mg/kg extract dosage increased the survival rate of 37% in SAM	Rajendran et al. (2010)
	Acetone	5.1	L	Neutralization lethal venom method	500 mg/kg extract dosage increased the survival rate of 87% in SAM	Rajendran et al. (2010)
	EtOH	5.1	AP	Neutralization lethal venom method	750 mg/kg extract dosage increased significant survival rate of 100% more than anti-venom itself in SAM	Shirwaikar et al. (2004)
Anti-viral	EtOH	5.1	AP	MIC	Active with MIC value of 0.01 mg/ml against VSV. Inactive against HSV type 1 virus	Ali et al. (1996)
Diuretic	MeOH	5.1	AP	Bioassay of diuretic	400 mg/kg of extract dosage increased urine volume of 77.42%, Na^+ (73.43%), K^- (83.38%) and Cl^- (25.83%) on AM	Das et al. (2005)
Estrogenic activity	PE	0.1	WP	Anti-estrogenic and estrogenic activity method	600 mg/kg extract dosage increased uterine weight of 71.98%, diameter of uterus (84.39%), thickness of endometrium (62.48%) and height of endometrial epithelium (66.00%) in AWR	Hiremath et al. (1999)
	EtOH	5.1	WP	Anti-estrogenic and estrogenic activity method	600 mg/kg extract dosage increased uterine weight of 50.76%, diameter of uterus (51.05%), thickness of endometrium (49.75%) and height of endometrial epithelium (50.89%) in AWR	Hiremath et al. (1999)
Hepatoprotective	EtOH	5.1	AP	Acetaminophen induced	100 mg/kg extract dosage decreased AST level of 35.44%, ALT (72.21%), ALP (74.97%) and MDH (52.92%). It also increased GSH (5.17%) and SOD (95.73%) in *WR*	Mathew et al. (2011)
	EtOH	5.1	L	Paracetamol induced	200 mg/kg extract dosage decreased SGOT level of 56.4% and SGPT (57.69%) in WM	Sutriana et al. (2010)
	EtOH	5.1	Unstated	Toxicity test	500 mg/kg extract dosage showed no significant difference on liver weight, ACP, ALP, AST, ALT and LDH level in AWR	Sathya et al. (2012)
	MeOH	5.1	AP	Thioacetamide induced toxicity	300 mg/kg extract dosage decreased GOT level of 57.00%, GPT (57.00%), ALKP (54.48%), TBL (38.76%) and CHL (58.29%). It also increased TPTN (93.70%) and ALB (87.91%) in AWR	Kumar et al. (2013)
Hypoxia	MeOH	5.1	L	Hypoxia induced rat	250 mg/kg extract dosage reduced MDA level of 30% in liver and 26% in plasma at SDR	Dwijayanti et al. (2015)
	Water	9.0	R	Hypoxia induce on nerve cell	20 mg/ml extract concentration increased neuron cell viability of 350.00%, BrdU (85.71%), BDNF (59.09%)	Ibrahim et al. (2012)
Neuro protective	Water	9.0	R	The extract was introduced before pancuronium bromide on frog gastrocnemius muscle and ischiadicus nerve	15–20 mg extract reduced spike from electrical stimuli on BF	Purwaningsih et al. (2010)
Neuro therapy activity	Water	9.0	R	Pancuronium bromide induce on frog gastrocnemius muscle and ischiadicus nerve then treated with extract	15–20 mg extract reduced spike from electrical stimuli on BF	Purwaningsih et al. (2010)
	Water	9.0	R	Pancuronium bromide induce on frog gastrocnemius muscle and ischiadicus nerve then treated with extract	15–20 mg extract reduced spike from electrical stimuli on BF	Andries (2009)
Post-coital antifertility effect	PE	0.1	WP	Anti-implantation method	600 mg/kg extract dosage increased the rate of no implantation up to 75.0% in AWR	Hiremath et al. (1999)
	Chloroform	4.1	WP	Anti-implantation method	Inactive	Hiremath et al. (1999)
	EtOH	5.1	WP	Anti-implantation method	600 mg/kg extract dosage increased the rate of no implantation up to 62.5% in AWR	Hiremath et al. (1999)
	Water	9.0	WP	Anti-implantation method	Inactive	Hiremath et al. (1999)
Toxicity	Hexane	0.0	AP	Green Fluorescent Protein (GFP) detection	5 µl extract was non-toxic to Vero cell line	Sanseera et al. (2012)

(continued on next page)

Table 10 *(continued)*

Activity tested	Extract	Polarity index[a]	Plant part	Model	Effect	Refs.
				method		
	Hexane	0.0	WP	Toxicity test	Lethality with LC_{50} value of 0.073 mg/ml in At	Hayati and Halimah (2012)
	Benzene	2.7	AP	Mosquito ovicidal activity method	No hatching of mosquito egg from the age of 0–115 days at a concentration of 0.2 mg/ml	Govindarajan et al. (2008a)
	Chloroform	4.1	AP	Mosquito ovicidal activity method	No hatching of mosquito egg from the age of 0–12 days at a concentration of 0.2 mg/ml	Govindarajan et al. (2008a)
	Chloroform	4.1	AP	Green Fluorescent Protein (GFP) detection methodology	5 μl extract was non-toxic to Vero cell line	Sanseera et al. (2012)
	Chloroform	4.1	WP	Toxicity test	Lethality with LC_{50} value of 0.057 mg/ml on At	Hayati and Halimah (2012)
	EA	4.4	AP	Mosquito ovicidal activity method	No hatching of mosquito egg from the age of 0–12 days at a concentration of 0.2 mg/ml	Govindarajan et al. (2008a)
	EtOH	5.1	AP	Microtitration toxicity assay	Toxic with CD_{50} value of 0.01 mg/ml on HeLa cell	Ali et al. (1996)
	EtOH	5.1	Unstated	Acute toxicity test	No sign of toxicity at a dosage of 2000 mg/kg on AWR	Sathya et al. (2012)
	EtOH	5.1	WP	Toxicity test	Lethality with LC_{50} value of 0.149 mg/ml on At	Hayati and Halimah (2012)
	EtOH	5.1	L	Toxicity experiment	Lethality with LC_{50} value of 0.026 mg/ml on Lc	Sharma et al. (2009)
	MeOH	5.1	AP	Green Fluorescent Protein (GFP) detection method	5 μl extract was non-toxic to Vero cell line	Sanseera et al. (2012)
	MeOH	5.1	AP	Mosquito ovicidal activity method	No hatching of mosquito egg from the age of 0–15 days at a concentration of 0.2 mg/ml	Govindarajan et al. (2008a)
	Water	9.0	L	Toxicity experiment	Lethality with LC_{50} value of 0.045 mg/ml on Lc	Sharma et al. (2009)
	Water	9.0	Unstated	Toxicity test	0.8 ml water from extract (150 g *Acalypha indica* in 50 ml water) killed 51.85% of Sl after 72 h	Ningsih et al. (2013)
Vasoconstrictor activity	PE	0.1	AP	Vasoconstrictor activity test	8.56 mg extract excited vasoconstrictor activity on frog blood vessel	Machineni et al. (2011)
	Chloroform	4.1	AP	Vasoconstrictor activity test	8.56 mg extract excited no vasoconstrictor activity on frog blood vessel	Machineni et al. (2011)
	EA	4.4	AP	Vasoconstrictor activity test	8.56 mg extract excited no vasoconstrictor activity on frog blood vessel	Machineni et al. (2011)
	EtOH	5.1	AP	Vasoconstrictor activity test	8.56 mg extract excited no vasoconstrictor activity on frog blood vessel	Machineni et al. (2011)
Wound healing	EtOH	5.1	Unstated	Excision wound model	10% w/v (extract in normal saline consisting 0.1% propylene glycol) increased wound healing rate of 24.37% on LAWR	Reddy et al. (2002)
	EtOH	5.1	Unstated	Resutured incision wound	10% w/v (extract in normal saline consisting 0.1% propylene glycol) increased strength of incision wound of 25.93% on LAWR	Reddy et al. (2002)
	70 Water: 30 EtOH	–	AP	Scratch assay	0.0001–0.1 mg/ml extracts healed scratches 10% faster on HSF cell	Ibrahim (2016)
	50 Water: 50 Ethanol	–	L	Excision and incision wound test	Healing rate at excision wound increased to 36% on W*R*	Ganeshkumar et al. (2012)

Ae = *Aedes aegypti*; Ah = *Aeromonas hydrophila*; Al = *Aspergillus flavus*; Am = *Aspergillus fumigatus*; AM = Albino mice; An = *Aspergillus niger*; AP = Aerial part; AR = Albino rat; As = *Anopheles stephensi*; At = *Artemia salina*; Av = *Alcaligenes viscolactis*; AWR = Albino wistar rat; Bc = *Bacillus cereus*; BF = *Bufo melanostictus*; Bm = *Bacillus megaterium*; Bs = *Bacillus subtilis*; Bsp = Bacillus species; Ca = *Candida albican*; Cg = *Candida glabrata*; Csp = Cytophaga species; Ct = *Candida tropicalis*; Ea = *Enterobacter aerogenes*; Ec = *Escherichia coli*; Ef = *Enterococcus faecalis*; El = *Enterobacter cloacae*; Hf = *Shigella flexneri*; HSV = Herpes simplex virus; Ka = *Klebsiella aerogenes*; Kp = *Klebsiella pneumoniae*; Ksp = Klebsiella species; L = Leaves; La = *Lactobacillus acidophilus*; LAWR = Lewis albino wistar rat; Lc = *Lymnaea acuminate*; MBC = Minimum bactericidal concentration; Mc = *Microsporum canis*; Md = *Salmonella enteritidis*; MIC = Minimum inhibitory concentration; Mm = *Salmonella typhimurium*; Mp = *Salmonella typhi*; Msp = Salmonella species; Mt = *Salmonella enterica*; Pa = *Pseudomonas aeruginosa*; Pc = *Penicillium chrysogenum*; Pp = *Pheretima posthuma*; Psp = Pseudomonas species; R = Root; Rf = *Streptococcus faecalis*; Rm = *Streptococcus mutans*; Rp = *Streptococcus pneumoniae*; Ry = *Streptococcus pyogenes*; Sa = *Staphylococcus aureus*; SAM = Swiss albino mice; SDR = Sprague Dawley rats; Se = *Staphylococcus epidermidis*; Sl = *Spodoptera litura*; Ssp = Staphylococcus species; Tm = *Proteus mirabilis*; Tv = *Proteus vulgaris*; Vc = *Vibrio cholera*, Vd = *Vibrio damsel*; VSV = Vesicular stomatitis virus; WM = White mouse; WP = Whole plant; W*R* = Wistar rat.

[a] Polarity index (Sadek, 2002).

Ravi, 2013; Savithramma et al., 2007; Senthilkumar et al., 2006), the attempt to conduct a scientific study using this plant is appreciated. Accordingly, Gupta et al. (2010) conducted an experiment with several tuberculosis bacteria using an aqueous extract of *Acalypha indica*. As a result, the mycobacterium tuberculosis H37Rv and two multi-drug resistance mycobacterium tuberculosis isolates; DKU-156 and JAL-1236, were inhibited by aqueous extract of *Acalypha indica*. However, the extract had a lower effect on the rapid growth of *Mycobacterium fortuitum* (TMC-1529) (Gupta et al., 2010). Chidambaram and Swaminathan (2013) also reported that all tuberculosis bacteria strains H-485, SH-577, SHOF-567 including H37Rv were not affected by the aqueous extract. An oral administration of this plant decoction could contribute minimally in treating this disease.

5.2.13. Anti-ulcer

There are phytochemicals inside the methanolic extract of *Acalypha indica* that are capable of inhibiting ulcer activity based on the treatment of the wistar rats (Kalimuthu et al., 2010). They discovered the ulcer inhibition activity by studying the reaction of pylorus ligature and swim stress in the rats. In their experiment, two concentrations of *Acalypha indica* were administered to the rats; 100 and 200 mg/kg per body weight. The standard drug reference for anti-ulcer activity is famotidine with 20 mg/kg per body weight at 5 ml/kg vehicle (5% w/v of acacia). The 200 mg/kg of extract reduced 77.14% of the volume of gastric juice, 69.29% of total acidity, 63.24% of free acidity, and 47.18% of ulcer index. For famotidine, the standard reduced the volume of gastric juice up to 82.14%, as well as total acidity (70.10%), free acidity (78.96%) and ulcer index (70.34%). The comparison between extract and standard showed that *Acalypha indica* has anti-ulcerogenic properties since the different value is small. Major phytochemicals in the extract such as the steroid and alkaloid provide a basic foundation for anti-ulcer activity (Kalimuthu et al., 2010). The extract inhibited gastric secretion and reduced pepsin activity in pylorus ligature and swim stress-induced ulcer in the rat. The people can consume the entirety of *Acalypha indica* to treat peptic ulcer disease as an alternative way to prescribing a synthetic drug.

5.2.14. Anti-urolithiasis

A stone formation in the urinary system comes from the hardened mineral deposited due to the high concentration inside the urine. The stone will interfere with the normal functions of the human urinary system and cause long-term pain. Therefore, Sathya et al. (2011) suggested a solution treatment for urolithiasis using natural resources and readily available plants such as *Acalypha indica*. The ethanolic extract of *Acalypha indica* has undergone biopotency on membrane-bound enzyme tests and marker enzymes tests on the urinary tract system of Wistar albino rats. The tests began with feeding the rats with water containing 0.75% ethylene glycol to induce calcium oxalate urolithiasis for 30 days. The trial treatment started with the introduction of *Acalypha indica* extract (200 mg/kg dose per day). The antioxidant phytochemicals inside the plant reacted with free radicals such as peroxyl, alkoxyl and aldehyde that caused severe damage to the membrane-bound enzyme (Pragasam et al., 2005). When the extract was used, the membrane-bound enzymes (Ca^{2+}, Mg^{2+} and $Na^{+}K^{+}$ ATPase) in the kidney and liver of urolithiases were given the equivalent of the standard drug, thiazide. The marker enzymes (ACP, ALP, AST and ALT) in serum, urine, kidney and liver at urolithiasis were maintained near normal concomitant with standard and lower than the untreated group. With this information, it was concluded that *Acalypha indica* can prevent kidney stone formation inside the human body through the anti-urolithiasis activity mechanism (Sathya et al., 2011).

5.2.15. Anti-venom

Shirwaikar et al. (2004) found that the anti-venom derived from *Acalypha indica* can treat *Daboia russelli* venom. By studying the venom-induced lethality, hemorrhage, necrotizing, and mast cell degranulation in rats, it was found that 750 mg/kg of ethanolic extract increased the survival rate up to 100% higher than the anti-venom itself. Later, Rajendran et al. (2010) studied other extracts from petroleum ether, benzene, chloroform, and acetone against similar snake venoms. The results showed that 500 mg/kg increased the survival rate of Swiss albino mice. The more polar phytochemicals extracted, the higher the survival rate. Meanwhile, petroleum ether, benzene, chloroform, and acetone increased the survival rate at 25%, 37%, 37%, and 87%, respectively. The antioxidant activity of the extract is one of the mechanisms of venom inactivation and inhibition (Alam et al., 1998). The *Daboia russelli* snake is found in Asian countries especially in India, Bangladesh, Sri Lanka, Nepal, Myanmar, and other countries within this area (McDiarmid et al., 1999). From studies conducted by Shirwaikar et al. (2004) and Rajendran et al. (2010), people living in that area could apply the emergency anti-venom remedy before the patient is taken to the hospital. Since the plant grows as a weed, it can be easily found in most communities and cities.

5.2.16. Anti-viral

A study was conducted by Ali et al. (1996) to find the inhibition activity of a virus from Malaysian indigenous plant medicines. Among the selected plants, *Acalypha indica* was tested against two types of Herpes simplex virus, Type 1 (HSV-1) and Vesicular stomatitis virus (VSV) on the HeLa cells. They used Minimum Inhibitory Concentration (MIC) to identify the anti-viral inhibition activity. From the results, HSV-1 virus was not affected by the *Acalypha indica* ethanol extract, while VSV virus was inhibited by ethanolic extract with a CD_{50} value of 0.01 mg/ml. Since VSV is RNA-type virus, they stated the cytotoxic and anti-VSV activities of extract may involve in the mode of action presumably through protein interaction (Ali et al., 1996). Further study is required with more virus species to gather more information related to *Acalypha indica* that can act as an anti-viral agent.

5.2.17. Diuretic

A previous study by Das et al. (2005) also showed that 400 mg/kg of methanolic extract increased urine volume by 77.42% after being introduced to the Albino mice. Frusemide was used as a standard positive control which showed a 72.72% increment when 20 mg/kg body weight was administered to the mice. The extract can excrete electrolytes such as Na^{+}, K^{+} and Cl^{-} higher than the standard drug. The results show the ability of *Acalypha indica* to be used as a diuretic drug. Only the aerial part is applicable for consumption as a natural diuretic medicine.

5.2.18. Estrogenic activity

Since petroleum ether and ethanol extract are the most effective, as derived from previous post-coital anti-fertility effect tests (Hiremath et al., 1999), both extracts have been subjected to anti-estrogenic activity tests. A standard drug reference used for the estrogenic activity test was ethynyl estradiol. In this test, six groups consisted of eight female albino rats; the first and second groups were negative and positive control groups. The second group was administered with a standard drug of 0.001 mg/rat per day. For the third and fourth groups, the rats received petroleum extract (600 mg/kg) and ethanol extract (600 mg/kg) while for the fifth and sixth groups, both standard drugs (0.001 mg/rat per day) were administered together with petroleum extract (600 mg/kg) and ethanol extract (600 mg/kg). Assessment for estrogenic activity was based on uterine weight, vaginal cornification, uterus diameter, endometrium thickness and endometrial epithelium height. Thus, a single administration of both 600 mg/kg petroleum and ethanol extracts presented weak estrogenic activity. However, the combination of standard and petroleum ether extract proved to have better anti-estrogenic activity than the standard alone (Hiremath et al., 1999). The sterol in petroleum ether extract was expected to be the responsible phytochemical that responded to

estrogenic activity. Two flavonoids found in the ethanolic extract; chrysin and galangin were expected to be the phytochemicals responsible for such therapeutic activity (Hiremath et al., 1998). By referring to Table 3, people used this plant for abortion and emmenagogue. This experiment proved the plant effectiveness in their practice. The whole plant consumption is recommended as emmenagogue while the leaves are suitable as a traditional abortion herb.

5.2.19. Hepatoprotective

The history of hepatoprotective study from *Acalypha indica* started in 2010 when Sutriana et al. (2010) applied ethanolic extract on the paracetamol induced Wistar mice. The 200 mg/kg dosage decreased SGOT by 56.4% and SGPT by 57.69% in mice blood. Both SGOT and SGPT will be released into the blood if the liver experiences damage. In this case, the damage came from the introduction of paracetamol by the researcher. Then, in 2011, Mathew et al. (2011) repeated a similar experiment with acetaminophen-induced Wistar rats. Sutriana et al. (2010) and Mathew et al. (2011) used a similar drug for the induction process because paracetamol is also known as acetaminophen. Mathew et al. (2011) recorded 35.44% of AST (SGOT) value and 72.21% of ALT (SGPT) decrement from 100 mg/kg of dosage administration. One year later, Sathya et al. (2012) conducted a toxicity test from *Acalypha indica* as a preparation to provide clinical data support and safety prescription dosage. They claimed there were no abnormalities in SGOT and SGPT values after the administration of up to 2000 mg/kg ethanolic extract into Albino wistar rats.

Later, Kumar et al. (2013) used 300 mg/kg of the methanolic extract on Albino wistar rats with thioacetamide to induce toxicity; both SGOT and SGPT levels decreased by 57%. These tests are actually a significant indicator for *Acalypha indica* as a potential herbal medicine for the hepatoprotective activity. Paracetamol (Acetaminophen) induction will release free radicals from liver oxidation that led to disturbance in the hepatocytes cell membrane. Hence, the SGOT and SGPT enzymes will be released and elevated in the serum as an indicator of liver damage (Nyblom et al., 2004). The hepatoprotective activity of *Acalypha indica* extract is caused by inhibition activity of cytochrome P_{450} and consequent glucuronidation along with its antioxidant effects. A similar induction drug was utilized in the study conducted by Kumar et al. (2013), which used thioacetamide for liver damage induction. The flavonoids in the extract are expected to play major roles as antioxidant phytochemicals for such activity. The use of a single extract without any liver damage induction proved to be of little significance on the hepatic activity (Sathya et al., 2012).

5.2.20. Hypoxia

An in vitro study by Ibrahim et al. (2012) on the nerve hippocampus cell of *Sprague Dawley* rats showed that the aqueous extract of the *Acalypha indica* root increased the mean relative of the neuron cell viability of up to 350% compared to the negative control group. The nerve cell treated by the extract underwent hypoxia induction before cell viability was measured. The level of cell proliferation was analyzed by BrdU labeling and BDNF quantification. The BrdU and BDNF levels increased together with neuron cell viability. Based on the results, they concluded the extract could improve rat hippocampal cells viability and endogenous BDNF level in hypoxic conditions. The antioxidant activity of kaempferol and tannin in the root extract counteracted with free radicals that caused neural impairment, preventing cell death.

Another experiment related to hypoxia was conducted via the in vivo method on the rats, where *Acalypha indica* was combined with *Centella asiatica* to enhance its effectiveness (Dwijayanti et al., 2015). The aim of their study was to prove the hepatoprotective effect from both plants in the inhibition activity of lipid peroxidation based on Malondialdehyde (MDA) level in plasma and liver against hypoxia. By measuring Malondialdehyde levels, they identified the combination of both herbs reduced the MDA value of 18.60% and 72.22% in the plasma and liver, respectively. The treatment using *Acalypha indica* and *Centella asiatica* alone decreased MDA levels down to 25% in plasma and 30% in the liver. Therefore, it was concluded that the combination of *Acalypha indica* and *Centella asiatica* was more effective. The best groups that showed a significant protective effect was 200 and 150 mg/kg per body weight of *Acalypha indica* and *Centella asiatica*, respectively. Since they used ethanol extract, which was like the solvent in hepatoprotective section studies, the similar mechanism of lipid peroxidation inhibition was adapted in this study. Furthermore, hypoxia also can generate reactive oxygen species that cause lipid peroxidation in the liver and plasma (Jusman et al., 2010). As a conclusion, the whole plant is highly recommended for treating hypoxia patients.

5.2.21. Neuroprotective activity

Purwaningsih et al. (2010) have conducted tests to see whether root aqueous extract possesses neuroprotective activity or not. According to their report, the extract was introduced in the frog gastrocnemius muscle and ischiadicus nerve followed by the pancuronium bromide. Then, they stimulated the nerve with an electrical source of 5 mV to study the extract effect. Finally, they claimed 20 mg of extract was capable of reducing the spike from electric stimuli on the frog muscle. However, their results show no statistical analysis for data justification. They can improve their experimental method to become more reliable with a more scientific approach especially at an electrical signal processing analysis. Meanwhile, their findings indirectly initiated a new potential study on this plant to be used as a neuroprotective drug. Purwaningsih et al. (2010) stated the stigmasterol compound was responsible for the neuroprotective activity since it was found in the root (Raj and Singh, 2000).

5.2.22. Post-coital anti-fertility effect

This plant has a post-coital anti-fertility effect according to the research conducted by Hiremath et al. (1999). The whole plant was extracted by petroleum ether, chloroform, ethanol, and distilled water for the in vivo test. Then, all crude extracts were administered to the female albino rats using the post-coital anti-fertility effect test. From the results, the petroleum ether and ethanol exhibited most post-coital anti-fertility effect at 300 and 600 mg/kg concentration per body weight. The rate of no implantation sites on the female rat increased up to 75.0% and 62.5% when the petroleum ether and ethanol extracts were used, respectively. They then continued the estrogenic activity experiment as discussed in Section 5.2.18. The anti-infertility effects discussed here may come from the flavonoids inside *Acalypha indica*; chrysin and galangin, (Hiremath et al., 1999). The petroleum ether extract contains several sterols which are expected to be responsible for the anti-fertility (Talapatra et al., 1981). Therefore, raw consumption of the whole plant is recommended for post-coital anti-fertility practice. Drinking water extract did not affect the implantation based on their study.

5.2.23. Vasoconstrictor activity

Machineni et al. (2011) have conducted a vasoconstrictor activity test on petroleum ether, chloroform, ethyl acetate and ethanolic extract from the aerial part of *Acalypha indica*. The test was done via ex vivo on the frog blood vessel. As a result, only the petroleum ether extract and the standard (Adrenaline) exhibited vasoconstrictor activity by reducing the liquid drop from the frog vessel due to constriction activity. The 8.56 mg petroleum ether extract was used to exhibit the constriction activity while only 0.3 mg for adrenaline. Inside their report, they stated the petroleum ether contained phytochemical groups from alkaloid, tannin, phenolic and saponin which might be responsible for such activity. They also mentioned the extract potential to treat primary disorders such as a headaches, migraines and diuretic. The data in Table 3 also shows the ethnomedicinal practices from India use this plant to treat headaches. The raw use of the aerial part of

Acalypha indica is suggested for vasoconstrictor therapeutic activity.

5.2.24. Wound healing

Reddy et al. (2002) confirmed that *Acalypha indica* has wound healing property as well as *Heliotropium indicum* and *Plumbago zeylanica* in their study. The ethanolic extract from the three plants was experimented on in the Albino wistar rats by using excision and incision wound models. The 10% w/v concentration of extract was prepared in a saline for topical application. The ethanolic extract of *Acalypha indica* required 18 days to completely heal a wound and has the lowest breaking strength from incision wound. The extract exhibited a 24.37% healing rate on the excision wound model and 25.93% on resutured incision wound. In their discussion section, they also mentioned the healing mechanism of *Acalypha indica* which has fair wound healing properties and low tensile strength, thus lowering the maturation rate of collagen (Reddy et al., 2002).

The other tests related to wound healing activity were also carried out by Ganeshkumar et al. (2012) and Ibrahim (2016). The extract from the mixed solvent (50% water: 50% ethanol) was tested on excision and incision wounds on the Wistar rat (Ganeshkumar et al., 2012). The healing rate for all wound models increased (36%) at better rates than Reddy et al. (2002). Ibrahim (2016) also used a mixed solvent (70% water: 30% ethanol) for extraction at the plant aerial part. The 0.1 mg/ml concentration of extract heals scratches 10% faster than the blank negative control. A detailed explanation of wound healing properties has already been discussed by Ganeshkumar et al. (2012) in their study. The ethanolic extract has significant wound healing potential by upregulating the genes of TNF-α and TNF-β which are very important cytokines for wound healing. The phytochemicals in the extract exhibit good antioxidant and nitric oxide scavenging activities, stimulating the healing factors at the wound (Balakrishnan et al., 2009). From these results, it can be concluded that *Acalypha indica* plant has useful phytochemicals for wound healing activities. According to Table 3, there are two methods to how the people from Oman and India consume this plant for wound healing medicine. The people in Oman eat this plant raw as medicine to treat wounds (Marwah et al., 2007). While in India, they mixed this plant with *Ficus benghalensis*, *Morus alba* and *Tridax procumbens* to produce would healing paste called Pasuru (Basha and Sudarshanam, 2011). For a common wound, the single use of *Acalypha indica* leaves is enough to heal the injury.

6. Discussion related to *Acalypha indica*

6.1. Raw uses

Section 2.2 explained the distribution of *Acalypha indica* in many areas in wet, temperate, tropical, and climate regions as a weed. Apart from that, many people from different countries take advantage of this plant and consume it for its many therapeutic purposes. This plant has been an alternative medicine for local people who tend to save on medicine. From Table 3, it can be seen that three major parts of the *Acalypha indica* can be used for ethnomedicinal treatment; leaves, root and the whole plant. From Fig. 2(B), most practices use this plant when it is still fresh, either as a single use or mixed with other ingredients. The raw fresh leaves contain the most active phytochemical from the original plant including its nutrients, essential oils and volatile compounds. The raw leaves are very useful for abortion since it has stigmasterol which affects estrogenic activity (Boldrin et al., 2013). The raw leaves can provide many benefits for several treatments when consumed orally including abortion, diarrhea, acts as an analgesic, emetic, and has, anti-inflammatory, anthelmintic, anti-bacterial, anti-cancer, anti-hyperlipidemic, anti-obesity, anti-oxidant, anti-tuberculosis, anti-venom, diuretic, hepatoprotective, vasoconstrictor, and wound healing properties. The volatile compound secreted by the leaf can treat a headache, ear aches, epilepsy, and act as an expectorant. The leaves can also be used topically as the following treatments; skin ailments, ganglion, hemorrhoids, constipation, insect bites, wound healing, and is anti-parasitic and anti-bacterial.

The root of the fresh *Acalypha indica* is useful as an anthelmintic and anti-arthritis through oral consumption. The root also acts as a neuro protective and wound healing agent through topical applications. The raw whole plant can be prepared for bronchitis treatment, emmenagogue, analgesic, diuretic, anti-bacteria, anti-diabetes, anti-inflammation, anti-oxidant, anti-ulcer, estrogenic, anti-urolithiasis and anti-implantation. Topical use from the fresh whole plant is suitable for wound treatment and external fungal infections for dermatology ailment. The combination of *Acalypha indica* with other remedies is dependent on practitioner knowledge to optimize the therapeutic effectiveness. The binder used in ethnomedicinal practice like oil or lime juice is useful for a homogeneous distribution of the phytochemicals, maintaining the crushed leaves shape, and increasing the treatment ability.

6.2. Water based uses

The aqueous extract is obtained by using water, a polar compound, as a solvent extractor from *Acalypha indica*. The extract has major soluble polar phytochemicals in water that are useful for several therapeutic purposes. The traditional practices usually use available surrounding resources including water as a part of the treatment ingredient. An herbal processing method like decoction relys on water, heat and simple cooking utensils and is applicable by everyone, everywhere without sophisticated instructions. Oral consumption of the leaf decoction is beneficial when prepared as an anthelmintic, anti-bacterial, anti-hyperlipidemic, anti-obesity, anti-oxidant, and anti-tubercular natural drug. The leaf decoction can also be applied to the patient who has a syphilitic ulcer, as practiced by people in India. Besides, the vaporized decoction can be used to treat asthma, ear aches, and headaches by rubbing around the ear and nose tip area. The root infusion in water has a good effect on healing hypoxia, arthritis, and acting as a laxative, and lowering blood sugar level. The root infusion can also be used on the nerve as a protective and therapeutic agent. Furthermore, the boiling water of the whole plant is intended for an aphrodisiac as well as treating ear aches and mouth ulcers.

6.3. Toxicity issue

Intoxication related to *Acalypha indica* has only occurred in livestock that foraged the weed for food (Nahrstedt et al., 1982). The symptoms exhibited by the intoxicated livestock were similar to victims of cyanide intoxication (Steyn, 1938). The cyanogenic phytochemical inside this plant will be hydrolyzed by the β-glucosidase enzyme before the production of sugars and cyanohydrin. The cyanohydrin will spontaneously decompose to HCN which is very poisonous to humans and livestock (Francisco et al., 2000). Without any specific prescription, uneducated individuals could easily be intoxicated by excessive consumption of the raw plant or drinking its juice. In Malaysia, some elders practice consuming this plant periodically and wait for the poison to be fully excreted from the body. They may not know of the cyanogenic compound but through past experiences, they know this plant has a certain amount of poison that not should be taken regularly. People around the world have been aware that *Acalypha indica* is toxic for a long time (Watt et al., 1962). Indeed, Acalyphin is the cyanogenic phytochemical presented in the *Acalypha indica* species responsible for such accident. There are seven types of cyanogenic phytochemicals, acalyphin, found in this plant. The major cyanogenic phytochemicals can be found at the leaves (roots 0.055%, stem 0.033%, leaves 0.350%, seed; not detectable) (Hungeling et al., 2009). Cyanide is lethal to humans if more than 1 mg/kg is consumed (New Zealand Food Safety Authority, 2016). Therefore, theoretically, if a person weighs 70 kg, they should not eat more than 20 g of raw leaves as it contains 70 mg of acalyphin.

In the studies conducted by Hungeling et al. (2009) and Nahrstedt et al. (1982), the acalyphin compound was detected and successfully isolated by using a fresh sample and methanol as the solvent extractor. Their studies involved no heat during extraction since a cold extraction method was applied. The cyanogenic phytochemical might be degraded if there is heat intervention during the preparation process as occurs on cassava cyanogenic phytochemical, linamarin (Ojo et al., 2013). Until now, no single study could figure out how to separate or reduce the cyanogenic effect from *Acalypha indica*. Raw consumption of the whole plant is the riskiest practice because people can be intoxicated. Even so, no records have been found of people dying to excessive consumption of *Acalypha indica*. Apart from that, the traditional practices use water as an extraction medium. Nobody has conducted any study on the number of cyanogenic phytochemicals inside *Acalypha indica* when they perform the therapeutic treatment. Since the plant is used as an aphrodisiac, there is the possibility of the risk of overdosing by uneducated people with obsessive behavior.

In Malaysia, some manufacturers have taken advantages of this situation by selling *Acalypha indica* as an instant coffee to the public (Malaysiakini, 2006). In the worst case scenarios, they exploit their product by adding a drug like sildenafil to enhance its effect. Consequently, the customers will suffer from an overdose of acalyphin and controlled drug leading to a risk of death. To prevent such an incident, the government has seized some *Acalypha indica* based instant coffees from the market and is strictly prohibiting any unregistered products; however, scholars and governments should work together by educating the public.

In order to examine the plant toxicity, various tests have been conducted regarding *Acalypha indica* toxicity level. The subjects for the toxicity tests began from in vitro tests using Vero cell lines (Sanseera et al., 2012) and HeLa cell lines (Ali et al., 1996). The toxicity test was also performed in Albino wistar rats through in vivo studies (Sathya et al., 2012). When this review paper was completed, four living organisms were tested in the toxicity study; *Anopheles stephensi* mosquito larvae (Govindarajan et al., 2008a), *Artemia salina* (Hayati and Halimah, 2012), *Spodoptera litura* (Ningsih et al., 2013), and *Lymnaea acuminate* (Sharma et al., 2009). Sanseera et al. (2012) claimed that 5 µl of hexane, chloroform and methanolic extract were non-toxic to the Vero cell line. The concentration used in their study was too low and not fully optimized to consider being justified. In another study by Ali et al. (1996), it was explained that the dosage of 0.01 mg/ml was the curative dose (CD_{50}) from the ethanolic extract from the aerial part of *Acalypha indica* on the HeLa cell line.

Sathya et al. (2012) stated that the ethanolic extract did not exhibit any intoxication symptoms on the Albino wistar rats even though the highest concentration was 2000 mg/kg per body weight. Although this may be true, no specific information discusses what the dosage suitable for human use is. Even in the discussion section, the researchers do not really emphasize the interaction between the extract and toxicity mechanism. In addition, the extract from *Acalypha indica* has also been tested with different living organisms to study their viability. *Artemia salina* is an aquatic crustacean, commonly used as a subject for toxicity tests due to low costs (Hayati and Halimah, 2012). In their test, three different extractor solvents have been utilized including chloroform, hexane, and ethanol. As a result, three of the extractions showed toxicity effect against *Artemia salina* with the lethal concentration (LC_{50}) chloroform, ethanol and hexane of 149.37, 73.46 and 57.09 ppm, respectively. Based on their judgment, all extractions have a bioactivity lethal potency since all values were below 1000 ppm. The water and ethanolic extracts are lethal to the *Lymnaea acuminate*, a freshwater snail, with the LC_{50} value of 0.026 mg/ml and 0.045 mg/ml (Sharma et al., 2009).

Ningsih et al. (2013) also presented in their report that 150 g of *Acalypha indica* in 50 ml water killed 51.85% of *Spodoptera litura*, an agriculture pest. They suggested the pesticide activity came from the phytochemical groups of flavonoids, steroid, saponin, and tannin found inside *Acalypha indica*. The toxicity effect on these organisms shows that *Acalypha indica* has the potential to be used as a green biology extermination agent. The cyanogenic compound inside *Acalypha indica* is suspected to be the killing agent that protects the plant from external threats (Francisco et al., 2000). In conclusion, the mode of toxicity mechanism on this organism might be different to the human biological system. To date, there is no supportive data available to relate the toxicity effect on the human with those organism's subjects from *Acalypha indica* cyanogenic compound.

6.4. Future study and applications

This plant is considered very cheap and free since it can be found in abundance. It has the potential to work as a therapeutic drug for many purposes based on the previous studies listed in Tables 3 and 10. The interested phytochemicals from the plant should be extracted, isolated and purified accordingly, depending on the therapeutic applications. This natural resource should be expanded and developed to become a secondary medicinal product, alternatively with available ones. As discussed above, this plant has several potentials uses for certain therapeutic activities which have proven to be better than standard prescribed drugs, particularly as an anthelmintic, anti-inflammatory, anti-bacterial, anti-cancer, anti-diabetes, anti-hyperlipidemic, anti-obesity, anti-venom, diuretic, hepatoprotective, and hypoxia and wound healing. From the discussion of pharmacology activities, most researchers highlight the antioxidants from this plant which exhibit very significant healing treatments especially as an analgesic, anti-urolithiasis, anti-venom, hepatoprotective, and hypoxia and wound healing activities. Table 5 shows there are eight flavonoids found in *Acalypha indica* which are expected to behave as antioxidant agents. Not only that, other phytochemicals such as ellagic acid, gallic acid and ascorbic acid also play an important role as antioxidant agents. There is also a possibility the concurrent effect from all antioxidant phytochemicals exhibits those therapeutic activities.

Recently, there are few types of research that have been conducted to use *Acalypha indica* for future medicine by synthesizing the plant extract with silver, copper and gold nanoparticles. The purpose of these studies was to treat cancer and develop an anti-bacterial agent (Krishnaraj et al., 2010, 2014; Manonmani et al., 2015; Sivaraj et al., 2014). The study of the *Acalypha indica* volatile phytochemicals and essential oils is still low and needs more exploration since it can be used to cure headaches and epilepsy through inhalation. People use this plant as an expectorant; unfortunately, the available information on the volatile phytochemicals and essential oils is insufficient. The other potential of *Acalypha indica* is its utilization as an exterminator agent for pest, molluscs and mosquito larvae. This bio-exterminator agent will hopefully be more environmentally-friendly than the synthetic product as the agent is developed naturally from the wild and safe for non-target organisms. Those who are interested in the therapeutic effects of *Acalypha indica* can further the study by identifying the responsible phytochemicals and its application area.

7. Conclusion

This review updates the information of *Acalypha indica* studies from several aspects such as phytochemical content, pharmacological activities, and ethnomedicinal practice from entire regions. The consumption of *Acalypha indica* as an ethnomedicinal herb has been discussed and associated with relevant pharmacological studies and phytochemical contents. The whole plant is applicable for treatment depending on the therapeutic activities. The preferred part of the plant for ethnomedicinal practice is its leaves, followed by whole plant and the root. For the optimum treatment effectiveness, a fresh plant is preferred. Studies have identified 24 pharmacological activities with some positive results. The most potential therapeutic treatments are as anthelmintic, anti-inflammatory, antibacterial, anti-cancer, anti-dia-

betes, anti-hyperlipidemic, anti-obesity, and anti-venom agents, is hepatoprotective, and has hypoxia and wound healing properties.

Instead of many therapeutic applications being practiced, the patient is still at risk of intoxication due to the cyanogenic compound in this plant. Further study using sequential polarity extraction is necessary to find which solvent has the most cyanogenic compound content solute from the plant. However, the interested compound may solute together with cyanogenic compounds during extraction causing the separation process of the compound to become more challenging. Another alternative solution regarding this issue is to study the effect of heat intervention with cyanogenic compound degradation. Since compound degradation is affected by heat, a study related to this factor is highly recommended.

Although the extracts have shown a positive reaction to many pharmacological studies activities, there is no recommended dosage prescribed for humans. This problem arises when the responsible compound inside the extract is not properly discussed and only depends on screening phytochemical tests. However, the available results are still applicable for estimation of the recommended dosage suitable for the patient. The next review should highlight the recommended dosage concluded from all gathering the results from all the studies.

Some pharmacological studies have shown a very good potential to be explored and furthered because the test results obtained have been almost comparable or better than the used standard. However, the test results are still not enough and should be supported by a few related tests including clinical trials. The responsible compound that reacts with the pharmacological studies should be isolated from the extract and purified for further analysis. There is a potential to find a new natural drug as an alternative to existing drugs.

There are some ethnomedicinal practices being applied that are not studied and explored by researcher although it is known to have been used by people for treatment. The pharmacological study of the practices is unexplicable and leaves questions regarding its functions. Therefore, this issue should be highlighted for future studies and researchers are encouraged to fill in this gap.

There are many types of research that can be done with this plant in the future since the supply resource of this plant is not an issue. This plant is considered as a low-cost herb and can easily grow with minimum preservation. Further studies related to *Acalypha indica* essential oil and volatile compound are highly recommended since as of yet there are no detailed studies of these compounds. The results from this study could answer questions regarding several ethnomedicinal practices, especially related to the inhalation method. For the future, many studies can be conducted to explore this plant's capabilities primarily related to therapeutic activities that have not been reviewed in this paper.

Acknowledgements

This work was financed by the research university grant (GUP), Universiti Teknologi Malaysia Q. J130000.2545.12H84 from Ministry of Higher Education (MOHE), Malaysia.

References

Aboubaker, D., Kelbessa, E., Hassan, S., Hassan-Abdallah, A., Djama, M., Asfaw, Z., Merito, A., 2013. Medicinal plants and their uses by the people in the region of Randa, Djibouti. J. Ethnopharmacol. 148, 701–713.

Ajaiyeoba, E., Onocha, P., Olarenwaju, O., 2001. In vitro anthelmintic properties of Buchholzia coriaceae and Gynandropsis gynandra extracts. Pharm. Biol. 39, 217–220.

Alam, M.I., Gomes, A., 1998. Viper venom-induced inflammation and inhibition of free radical formation by pure compound (2-hydroxy-4-methoxy benzoic acid) isolated and purified from anantamul (*Hemidesmus indicus* R. BR) root extract. Toxicon 36, 207–215.

Ali, A.M., Mackeen, M.M., El-Sharkawy, S.H., Abdul Hamid, J., Ismail, N.H., Ahmad, F., Lajis, M.N., 1996. Antiviral and cytotoxic activities of some plants used in Malaysian indigenous medicine. Pertanika J. Trop. Agric. Sci. 19, 129–136.

Amarnath, K., Dhanabal, J., Agarwal, I., Seshadry, S., 2014. Cytotoxicity induction by ethanolic extract of *Acalypha indica* loaded casein-chitosan microparticles in human prostate cancer cell line in vitro. Biomed. Prev. Nutr. 4, 445–450.

Ameenah Gurib-Fakim, Guého, J., 1996. Plantes Médicinal de Maurice Edition de L'Ocean Indien ed. Mauritius.

Andries, G., 2009. Efek neuroterapi ekstrak air akar *Acalypha indica* Linn. dosis 15 dan 20 mg secara eks vivo pada persambungan saraf-otot gastroknemius katak *Bufo melanostictus Schneider*, Fakultas Kedokteran. Universitas Indonesia, Indonesia.

Awoyinka, O., Balogun, I., Ogunnowo, A., 2007. Phytochemical screening and in vitro bioactivity of *Cnidoscolus aconitifolius* (Euphorbiaceae). J. Med. Plants Res. 1, 063–065.

Azmahani, A., Somchit, M., Rosyilah, A., 2002. In vitro anti-bacterial and anti-fungal properties of *Acalypha indica* (Kucing Galak). In: Proceedings of the Regional Symposium on Environment and Natural Resources. Malaysia, pp. 503–508.

Baharum, N.N., 2015. Analysis of *Acalypha indica* Extracts for Antioxidant and Antibacterial Activities. Department of Biosciences and Health Sciences, Universiti Teknologi, Malaysia.

Balakrishnan, N., Panda, A., Raj, N., Shrivastava, A., Prathani, R., 2009. The evaluation of nitric oxide scavenging activity of *Acalypha indica* Linn root. Asian J. Res. Chem. (AJRC). 2, 148–150.

Basha, S.K., Sudarshanam, G., 2011. Multiple herbal therapy-antimicrobial activity of wound healing paste (Pasuru) used by Sugali tribes of Yerramalais of Kurnool District. Int. J. Pharm. Sci. Res. 3, 1238–1241.

Batubara, I., Wahyuni, W.T., Firdaus, I., 2016. Utilization of anting-anting (*Acalypha indica*) leaves as antibacterial. In: Proceedings of the IOP Conference Series: Earth and Environmental Science. IOP Publishing, p. 012038.

Boldrin, P.K., Resende, F.A., Höhne, A.P.O., de Camargo, M.S., Espanha, L.G., Nogueira, C.H., Maria do Socorro, F.M., Vilegas, W., Varanda, E.A., 2013. Estrogenic and mutagenic activities of *Crotalaria pallida* measured by recombinant yeast assay and Ames test. BMC Complement. Altern. Med. 13, 216.

Burkill, H.M., 1994. The Useful Plants of West Tropical Africa 2. Families EI. Royal Botanic Gardens.

Chengaiah, B., Mahesh Kumar, K., Alagusundaram, M., Sashikala, C., Madhusudhana Chetty, C., 2009. In vitro anthelmintic activity of roots of *Acalypha indica* Linn. Int. J. PharmTech Res. 1, 1499–1502.

Chidambaram, S., Swaminathan, R., 2013. Determination of anti-tubercular activity of four indian medicinal plants against mycobacterium tuberculosis by broth micro dilution method. Int J. Pharm. Sci. Res., 4.

Chitravadivu, C., Manian, S., Kalaichelvi, K., 2009. Qualitative analysis of selected medicinal plants, Tamilnadu, India. Middle-East J. Sci. Res. 4, 144–146.

Chopra, R., Nayar S.I., IC, C., 1956. Glossary of Indian Medical Plants. New Delhi, India.

Crunkhorn, P., Meacock, S., 1971. Mediators of the inflammation induced in the rat paw by carrageenin. Br. J. Pharmacol. 42, 392–402.

Das, A., Ahmed, F., Biswas, N., Dev, S., Masud, M., 2005. Diuretic activity of *Acalypha indica*. Dhaka university. J. Pharm. Sci., 4.

Das, P.R., Akter, S., Islam, M.T., Kabir, M.H., Haque, M.M., Khatun, Z., Nurunnabi, M., Khatun, Z., Lee, Y.-k., Jahan, R., 2012. A selection of medicinal plants used for treatment of diarrhea by folk medicinal practitioners of Bangladesh. Am.-Eurasia. Sustain. Agric. 6, 153–161.

Devi, D.K., Raj, A.V., 2013. antibacterial potential, phytochemical investigation And characterization Of antibacterial protein Of different fractions Of *Acalypha indica*. Int. J. Pharm. Sci. Res. 4, 445–452.

Dineshkumar, B., Vigneshkumar, P., Bhuvaneshwaran, S., Analava, M., 2010. Phyto-pharmacology of *Acalypha indica*: a review. Int. J. Biosci. Altern. Holist. Med. (IJBSAHM). 1, 27–32.

Discoverlife, 2015. *Acalypha indica*. Discoverlife, USA. Available from: ⟨http://www.discoverlife.org/mp/20m?Kind=Acalypha+indica⟩. (Accessed 5 June 2016).

Divya, N., Thenmozhi, S., Sureshkumar, B., Selvan, M., 2014. Antibacterial activity of medicinal plant against wound infected pathogens. Int. J. Pharm. Sci. Res. 5, 4942–4947.

Duke, J., 2016. Dr. Duke's Phytochemical and Ethnobotanical Databases. U.S. Department of Agriculture, Agricultural Research Service. Available from: ⟨http://dx.doi.org/10.15482/USDA.ADC/1239279⟩. (Accessed 5 March 2017).

Dwijayanti, A., Frethernety, A., Hardiany, N.S., Purwaningsih, E.H., 2015. Hepatoprotective effects of *Acalypha indica* and *Centella asiatica* in rat's liver against hypoxia. Procedia Chem. 14, 11–14.

Falodun, A., Ali, S., Quadir, I.M., Choudhary, I.M., 2008. Phytochemical and biological investigation of chloroform and ethylacetate fractions of *Euphorbia heterophylla* leaf (Euphorbiaceae). J. Med. Plants Res. 2, 365–369.

Francisco, I.A., Pinotti, M.H.P., 2000. Cyanogenic glycosides in plants. Braz. Arch. Biol. Technol. 43, 487–492.

Ganeshkumar, M., Ponrasu, T., Krithika, R., Iyappan, K., Gayathri, V.S., Suguna, L., 2012. Topical application of *Acalypha indica* accelerates rat cutaneous wound healing by up-regulating the expression of Type I and III collagen. J. Ethnopharmacol. 142, 14–22.

Ghani, A., 2003. Medicinal Plants of Bangladesh: Chemical Constituents and Uses 2nd ed ed.. Asiatic Society of Bangladesh, Dhaka.

Giday, M., Teklehaymanot, T., 2013. Ethnobotanical study of plants used in management of livestock health problems by Afar people of Ada'ar District, Afar Regional State, Ethiopia. J. Ethnobiol. Ethnomed. 9, 8.

Govindarajan, M., Jebanesan, A., Pushpanathan, T., Samidurai, K., 2008a. Studies on effect of *Acalypha indica* L.(Euphorbiaceae) leaf extracts on the malarial vector, *Anopheles stephensi* Liston (Diptera: culicidae). Parasitol. Res. 103, 691–695.

Govindarajan, M., Jebanesan, A., Reetha, D., Amsath, R., Pushpanathan, T., Samidurai, K., 2008b. Antibacterial activity of *Acalypha indica* L. Eur. Rev. Med. Pharmacol.

Sci. 12, 299–302.
Guo, X.-D., Ma, Y.-J., Parry, J., Gao, J.-M., Yu, L.-L., Wang, M., 2011. Phenolics content and antioxidant activity of tartary buckwheat from different locations. Molecules 16, 9850–9867.
Gupta, R., Thakur, B., Singh, P., Singh, H., Sharma, V., Katoch, V., Chauhan, S., 2010. Anti-tuberculosis activity of selected medicinal plants against multi-drug resistant Mycobacterium tuberculosis isolates. Indian J. Med. Res. 2010, 809–813.
Gurib-Fakim, A., 2011. Medicinal Plants of Mauritius and of the World. Caractère Ltèe, Mauritius.
Hayati, E.K., Halimah, Nur, 2012. Phytochemical test and brine shrimp lethality test against *Artemia salina* Leach of Anting-anting (*Acalypha indica* Linn.) plant extract. Alchemy 1 (2), 53–103.
Henry, A., Hosagoudar, V., Ravikumar, K., 1996. Ethno-medico-botany of the Southern Western Ghats of India. Ethnobiology in Human Welfare. Deep Publications, New Delhi.
Hiremath, S., Rudresh, K., Badami, S., 1998. Flavonoids of *Acalypha indica* Linn. Indian J. Heterocycl. Chem. 8, 163–164.
Hiremath, S.P., Rudresh, K., Badami, S., Patil, S.B., Patil, S.R., 1999. Post-coital antifertility activity of *Acalypha indica* L. J. Ethnopharmacol. 67, 253–258.
Hnatyszyn, O., Juárez, S., Ouviña, A., Martino, V., Zacchino, S., Ferraro, G., 2007. Phytochemical analysis and antifungal evaluation of *Sebastiania commersoniana*. extracts. Pharm. Biol. 45, 404–406.
Hungeling, M., Lechtenberg, M., Fronczek, F.R., Nahrstedt, A., 2009. Cyanogenic and non-cyanogenic pyridone glucosides from *Acalypha indica* (Euphorbiaceae). Phytochemistry 70, 270–277.
Hussain, A.Z., Kumaresan, S., 2013. GC-MS analysis and antibacterial evaluation of *Acalypha indica*. Asian J. Plant Sci. Res. 3, 46–49.
Ibrahim, A.M., 2016. In Vitro Evaluation and Wound Healing Cream Formulation of *Acalypha indic*a Linn Ethanolic Extract. Department of Biosciences and Health Sciences, Universiti Teknologi, Malaysia.
Ibrahim, N., Rahadian, J., Suniarti, D.F., 2012. *Acalypha indica* Linn root extract improved hippocampal cell viability and increased brain-derived neurotrophic factor (BDNF) in hypoxic condition. Med. J. Indones. 21, 141.
Integrated Taxonomic Information System, 2015. *Acalypha indica* L. Available from: ⟨http://www.itis.gov/servlet/SingleRpt/SingleRpt?Search_topic=TSN & search_value=28185⟩.(Accessed 15 October 2015).
Isman, M.B., 2000. Plant essential oils for pest and disease management. Crop Prot. 19 (8), 603–608.
Jayaprakasam, R., Ravi, T., 2013. Evaluation of anti arthritic activity of the root extract of *Acalypha indica* Linn. using in vitro techniques. Int. J. Phytopharm. 2, 169–173.
Joy, B., Mathew, M., Awaad, A., Govil, J., Singh, V., 2010. Anti-oxidant studies and chemical investigation of ethanol extract of *Acalypha indica* Linn. Drug Plants I, 261–279.
Junior, A., Zanil, C., 2000. Biological screening of Brazilian meditational plants. Braz. J. Sci., 367–373.
Jusman, S.A., Halim, A., 2010. Oxidative stress in liver tissue of rat induced by chronic systemic hypoxia. Makara J. Health Res., 34–38.
Kalimuthu, S., Rajesh, P., Kannan, V.R., Balamurugan, B., Chandrasekar, T., 2010. Antiulcer activity of methanolic extract of *Acalypha indica* Linn. (Euphorbiaceae) by pylorous ligture and swim stress induced ulceration. J. Pharm. Res. 3, 2779–2783.
Kamalakannan, S., Murugan, K., Barnard, D.R., 2011. Toxicity of *Acalypha indica* (Euphorbiaceae) and *Achyranthes aspera* (Amaranthaceae) leaf extracts to *Aedes aegypti* (Diptera: culicidae). J. Asia-Pac. Entomol. 14, 41–45.
Kankanamalage, T., Dharmadasa, R., Abeysinghe, D., Wijesekara, R., 2014. A survey on medicinal materials used in traditional systems of medicine in Sri Lanka. J. Ethnopharmacol. 155, 679–691.
Khrisnan, N., Jeyachandran, A., Nagendran, N., 2000. Effect of seasonal and altitudinal variations on growth performance of Acalypha indica Linn. in Alagar Hill (Eastern Ghats), South India. Trop. Ecol. 41, 41–45.
Kirtikar, K.R.B., Baman, D., 1918. Indian medicinal plants. Indian Med. Plants.
Krishnaraj, C., Jagan, E., Rajasekar, S., Selvakumar, P., Kalaichelvan, P., Mohan, N., 2010. Synthesis of silver nanoparticles using *Acalypha indica* leaf extracts and its antibacterial activity against water borne pathogens. Colloids Surf. B: Biointerfaces 76, 50–56.
Krishnaraj, C., Muthukumaran, P., Ramachandran, R., Balakumaran, M., Kalaichelvan, P., 2014. *Acalypha indica* Linn: biogenic synthesis of silver and gold nanoparticles and their cytotoxic effects against MDA-MB-231, human breast cancer cells. Biotechnol. Rep. 4, 42–49.
Kumar, D., Kumar, A., Prakash, O., 2012. Potential antifertility agents from plants: a comprehensive review. J. Ethnopharmacol. 140, 1–32.
Kumar, S.S., Kumar, C.V., Vardhan, A.V., 2013. Hepatoprotective activity of *Acalypha indica* Linn against thioacetamide induced toxicity. Int J. Pharm. Pharm. Sci. 5, 3–7.
Lingaraju, D., Sudarshana, M., Rajashekar, N., 2013. Ethnopharmacological survey of traditional medicinal plants in tribal areas of Kodagu district, Karnataka, India. J. Pharm. Res. 6, 284–297.
Ma, Y.T., Chuang, J.I., Lin, J.H., Hsu, F.L., 1997. Phenolics from *Acalypha indica*. J. Chin. Chem. Soc. 44, 499–502.
Machineni, K.M., Rao, M.P., Rao, V.N., Bhogavalli, K., Praveen, B., 2011. Studies on phytochemical screening and vasoconstrictor activity of leaf extracts of *Acalypha indica* on frog blood vessels. Ann. Biol. Res., 2.
Maji, S., Dandapat, P., Ojha, D., Maity, C., Halder, S., Mohapatra, P.D., Pathak, T., Pati, B., Samanta, A., Mondal, K., 2010. In vitro antimicrobial potentialities of different solvent extracts of ethnomedicinal plants against clinically isolated human pathogens. J. Phytol., 2.
Malaysia Peninsular Forestry Department, 2017. *Acalypha indica*. Available from: ⟨http://www.forestry.gov.my/index.php/my/jpsm/index.php/my/pusat-sumber/berita/9-explore/996-acalypha-indica⟩. (Accessed 30 January 2017).
Malaysiakini, 2006. Kaji pokok Kucing Galak tambah oomph lelaki. Malaysiakini, Malaysia. Available from: ⟨http://www.malaysiakini.com/news/47128⟩. (Accessed 30 January 2017).
Manonmani, P., Ramar, M., Geetha, N., Valan Arasu, M., Raskin Erusan, R., Mariselvam, R., Sowmiya, J.J., 2015. Synthesis of silver nanoparticles using natural products from acalypha indica (kuppaimeni) and curcuma longa (turmeric) on antimicrobial activities. Int. J. Pharm. Res. Bio-Sci. 4, 151–164.
Martin, G.J., 1995. Ethnobotany – A People and Plants Conservation Manual. Parthenon Publishing Group Casterton Hall, Carnforth Lancashire, England.
Marwah, R.G., Fatope, M.O., Al Mahrooqi, R., Varma, G.B., Al Abadi, H., Al-Burtamani, S.K.S., 2007. Antioxidant capacity of some edible and wound healing plants in Oman. Food Chem. 101, 465–470.
Masih, M., Banerjee, T., Banerjee, B., Pal, A., 2011. Antidiabetic activity of *Acalypha indica* Linn. on normal and alloxan induced diabetic rats. Int. J. Pharm. Pharm. Sci. 3, 51–54.
Mathew, M., Nair, C., Shenoy, T., Varghese, J., 2011. Preventive and curative effects of *Acalypha indica* on acetaminophen-induced hepatotoxicity. Int. J. Green. Pharm. 5, 49.
McDiarmid, R.W., Campbell, J.A., Touré, T., 1999. Snake Species of the World: A Taxonomic and Geographic Reference. v. 1.
Mohan, C., Dinakar, S., Anand, T., Elayaraja, R., SathiyaPriya, B., 2012. Phytochemical, GC-MS analysis and antibacterial activity of a medicinal plant *Acalypha indica*. Int. J. Pharm. Tech. Res. 4, 1050–1054.
Moon, J., Do, H.-J., Kim, O.Y., Shin, M.-J., 2013. Antiobesity effects of quercetin-rich onion peel extract on the differentiation of 3T3-L1 preadipocytes and the adipogenesis in high fat-fed rats. Food Chem. Toxicol. 58, 347–354.
Moscow, S., Jothivenkatachalam, K., 2012. Study on mineral content of some Ayurvedic Indian medicinal plants. Int. J. Pharma. Sci. Res. (IJPSR) 3, 294–299.
Mucignat-Caretta, C., Poddar-Sarkar, M., Brahmachary, R.L., 2014. Pheromones of tiger and other big cats. In: Mucignat-Caretta, C. (Ed.), Neurobiology of Chemical Communication. CRC Press, Boca Raton (FL).
Murugan, P.S., Selvam, G.S., 2015. Identification and quantification of phytocompounds in *Acalypha indica* leaves. Int. J. Pharm. Bio-Sci. 6, 11–21.
Mutheeswaran, S., Pandikumar, P., Chellappandian, M., Ignacimuthu, S., 2011. Documentation and quantitative analysis of the local knowledge on medicinal plants among traditional Siddha healers in Virudhunagar district of Tamil Nadu, India. J. Ethnopharmacol. 137, 523–533.
Muthuvelan, B., Raja, R.B., 2008. Studies on the efficiency of different extraction procedures on the anti microbial activity of selected medicinal plants. World J. Microbiol. Biotechnol. 24, 2837–2842.
Muzammil, M.S., Manikandan, M., Jafar, A., Sakthivel, P., Geetha, S., Malarkodi, R., 2015. Anti-inflammatory studies on *Acalypha indica* L. leaves by membrane stabilization. Indian J. Nat. Prod. Resour. (IJNPR) [Former. Nat. Product. Radiance (NPR)] 5, 195–197.
Nadakarni, K.M., Nadakarni, A.M., 1982. The Indian Medicinal Plants. Popular Prakashan, Bombay.
Nahrstedt, A., Hungeling, M., Petereit, F., 2006. Flavonoids from *Acalypha indica*. Fitoterapia 77, 484–486.
Nahrstedt, A., Kant, J.-D., Wray, V., 1982. Acalyphin, a cyanogenic glucoside from *Acalypha indica*. Phytochemistry 21, 101–105.
Nandhakumar, M., Tamil Iniyan, G., Senthilkumar, M., Dineshkumar, B., Mitra, A., 2009. In vitro assay of alpha amylase inhibitory activity of Indian medicinal herb *Acalypha indica*. J. Clin. Diagn. Res. 3, 1475–1478.
Nasir, A.G., 2012. Pengamal perubatan tradisional melayu tidak pernah jalani latihan formal. Universiti Kebangsaan Malaysia, Malaysia. Available from: ⟨http://www.ukm.my/news/arkib/tahun-2012/oktober-2012/pengamal-perubatan-tradisional-melayu-tidak-pernah-jalani-latihan-formal/⟩. (Accessed 27 February 2017).
National Institute of Arthritis and Musculoskeletal and Skin Disease, N, 2014. Arthritis and Rheumatic Disease. National Institute of Arthritis and Musculoskeletal and Skin Disease, USA. Available from: ⟨https://www.niams.nih.gov/Health_Info/Arthritis/arthritis_rheumatic.asp⟩. (Accessed 12 March 2017).
NaturalMedicineFacts.info, 2017. *Acalypha indica* health effects and herbal facts.
Nelson, R.H., 2013. Hyperlipidemia as a risk factor for cardiovascular disease. Prim. Care. 40, 195–211.
New Zealand Food Safety Authority, N, 2016. Cyanogenic Glycoside – Information Sheet. Available from: ⟨www.foodsafety.govt.nz/elibrary/industry/Cyanogenic_Glycosides-Toxin_Which.pdf⟩. (Accessed 24 June 2016).
Ningsih, T.U.U., Yuliani, Y., Haryono, T., 2013. Pengaruh filtrat umbi gadung, daun sirsak dan herba anting-anting terhadap mortalitas larva *Spodoptera litura*. LenteraBio, 2.
Noriko, N., 2013. Potensi daun teh (*Camellia sinensis*) dan daun Anting-anting *Acalypha indica* L. dalam menghambat pertumbuhan *Salmonella typhi*. Seri Sains Dan. Teknol. 2, 104–110.
Nyblom, H., Berggren, U., Balldin, J., Olsson, R., 2004. High AST/ALT ratio may indicate advanced alcoholic liver disease rather than heavy drinking. Alcohol. Alcohol. 39, 336–339.
Ocktarini, R., 2010. Pengaruh ekstrak herba anting-anting (*Acalypha australis* L.) terhadap kadar glukosa darah mencit Balb/C induksi streptozotocin. Universitas Sebelas Maret, Surakarta, Indonesia.
Ojo, R.J., Obi, N.P., Akintayo, C.O., Adebayo-Gege, G.I., 2013. Evaluation of cyanogen contents of cassava and cassava based food products in Karu, Nasarawa state, North central Nigeria. J. Environ. Sci., Toxicol. Food Technol. 6, 47–50.
Paindla, P., Mamidala, E., 2014. Phytochemical and chromatographic studies in the leaves extract of *Acalypha indica*. Online Int. Interdiscip. Res. J. 4, 175–182.
Pavelka, K., Forejtová, Š., Olejarova, M., Gatterova, J., Šenolt, L., Špaček, P., Braun, M.,

Hulejova, M., Štovíčková, J., Pavelkova, A., 2004. Hyaluronic acid levels may have predictive value for the progression of knee osteoarthritis. Osteoarthr. Cartil. 12, 277–283.
Peres, M.T., Delle Monache, F., Cruz, A.B., Pizzolatti, M.G., Yunes, R.A., 1997. Chemical composition and antimicrobial activity of *Croton urucurana* Baillon (Euphorbiaceae). J. Ethnopharmacol. 56, 223–226.
Pragada, R., Vangepurapu, V., Ethadi, S., Praneeth, V., 2011. Phytochemical investigation and in vitro anti oxidant, anti microbial activity of different fractions of *Acalypha indica* Linn. Int. J. Pharm. Pharm. Sci. 3, 314–317.
Pragasam, V., Kalaiselvi, P., Sumitra, K., Srinivasan, S., Varalakshmi, P., 2005. Counteraction of oxalate induced nitrosative stress by supplementation of L-arginine, a potent antilithic agent. Clin. Chim. Acta 354, 159–166.
Purushothaman, K.K., Chandrasekharan, S., Kalyani, K., 1973. J. Res. Indian Med. 8, 50.
Purwaningsih, E.H., Ibrahim, N., Zain, H., Tedjo, A., 2010. Neuro-protection and neuro-therapy effects of *Acalypha indica* Linn. water extract ex vivo on Musculus gastrocnemius frog. MAKARA Health Ser., 12.
Rahman, M.A., Bachar, S.C., Rahmatullah, M., 2010. Analgesic and anti-inflammatory activity of methanolic extract of *Acalypha indica* Linn. Pak. J. Pharm. Sci. 23, 256–258.
Raj, J., Singh, K.P., 2000. Acalypha Indica 22 (21–22), 21–26.
Rajasekaran, S., Anandan, R., Nishad, K., 2013. Antihyperlipidemic activity of *Acalypha indica* Linn. on atherogenic diet induced hyperlipidemia. Int. J. Pharm. Pharm. Sci. 5, 699–701.
Rajaselvam, J., Benila, S., Meena, R., 2012. Study of antimicrobial activity of *Acalypha Indic*a against selected microbial species. Int. J. Pharm. Sci. Res. 3, 473–476.
Rajendran, K., Shirwaikar, A., Mehta, M., Bharathi, R.V., 2010. In vitro and in vivo anti-snake venom (*Daboia russelli*) studies on various leaf extracts of *Acalypha indica* Linn. Int. J. Phytomed., 2.
Rampilla, V., Mahammad, K.S., 2015. Ethno-Medicinal plants in sacred groves in east Godavari District, Andhra Pradesh, India. Eur. J. Med. Plants, 9.
Ranju, G., Niranjan, S., Kumar, P.S., Kumar, P.V., Kumar, P.S., 2011. In vitro anthelmintic activity of *Acalypha indica* leaves extracts. Int. J. Res. Ayurveda Pharmacol. 2, 247–249.
Rao, R., 1996. Traditional knowledge and sustainable development: key role of ethnobiologists. Ethnobotany 8, 14–24.
Rastogi, R.P., Mehrotra, B., 1990. Compendium of Indian Medicinal Plants. Central Drug Research Institute.
Reddy, J.S., Rao, P.R., Reddy, M.S., 2002. Wound healing effects of *Heliotropium indicum*, *Plumbago zeylanicum* and *Acalypha indica* in rats. J. Ethnopharmacol. 79, 249–251.
Reddy, K., Trimurthulu, G., Reddy, C.S., 2010. Medicinal plants used by ethnic people of Medak district, Andhra Pradesh. Indian J. Tradit. Knowl. 9, 184–190.
Ribeiro, A., Romeiras, M.M., Tavares, J., Faria, M.T., 2010. Ethnobotanical survey in Canhane village, district of Massingir, Mozambique: medicinal plants and traditional knowledge. J. Ethnobiol. Ethnomed. 6, 33.
Ruslan, N.F., 2015. Evaluation of *Acalypha indica* Extracts for Antioxidant and Antibacterial Activities. Department of Biosciences and Health Sciences, Universiti Teknologi, Malaysia.
Sadek, P.C., 2002. The HPLC Solvent Guide 2nd edition. John WIley and Sons.
Saha, R., Ahmed, A., 2011a. Hypoglycemic effect of *Acalypha indica* Linn. plant extracts on streptozotocin induced diabetes in rat. Int. J. Pharm. Sci. Res. 2, 2934–2937.
Saha, R., Ahmed, A., 2011b. Phytochemical constituents and pharmacological activities of *Acalyphus indica* Linn: a review. Int. J. Pharm. Sci. Res. 2, 1900–1904.
Sakthi, S.S., Geetha, M., Saranraj, P., 2011. Pharmacological screening of *Datura metel* and *Acalypha indica* for its antifungal activity against pathogenic fungi. Int. J. Pharm. Sci. Health Care. 2, 15–30.
Samy, R.P., Ignacimuthu, S., Raja, D.P., 1999. Preliminary screening of ethnomedicinal plants from India. J. Ethnopharmacol. 66, 235–240.
Sanseera, D., Niwatananun, W., Liawruangrath, B., Liawruangrath, S., Baramee, A., Trisuwan, K., Pyne, S.G., 2012. Antioxidant and anticancer activities from aerial parts of *Acalypha indica* Linn. Chiang Mai Univ. J. Nat. Sci. 11 (2), 157–168.
Saranraj, P., Stella, D., Sathiyaseelan, K., Samuel, S., 2010. Antibacterial potentiality of ethanol and ethyl acetate extract of *Acalypha indica* against human pathogenic bacteria. J. Ecobiotechnol., 2.
Sathya, M., Kokilavani, R., Teepa, K., 2012. Acute and subacute toxicity studies of ethanolic extract of *Acalypha indica* Linn in male wistar albino rats. Asian J. Pharm. Clin. Res..
Sathya, M., Kokilavani, R., Teepa, K.A., Balakrishnan, A., 2011. Biopotency of *Acalypha indica* Linn on membrane bound ATPases and marker enzymes urolithic rats. Anc. Sci. Life 31, 3.
Savithramma, N., Sulochana, C., Rao, K., 2007. Ethnobotanical survey of plants used to treat asthma in Andhra Pradesh, India. J. Ethnopharmacol. 113, 54–61.
Scaffidi, A., Algar, D., Bohman, B., Ghisalberti, E.L., Flematti, G., 2016. Identification of the cat attractants Isodihydronepetalactone and Isoiridomyrmecin from *Acalypha indica*. Aust. J. Chem. 69, 169–173.
Schmelzer, G.H., 2007. *Acalypha indica* L., Wageningen, Netherland. Available from: ⟨http://www.database.prota.org/PROTAhtml/Acalypha%20indica_En.htm⟩. (Accessed 20 August 2014).
Seebaluck, R., Gurib-Fakim, A., Mahomoodally, F., 2015. Medicinal plants from the genus Acalypha (Euphorbiaceae)–a review of their ethnopharmacology and phytochemistry. J. Ethnopharmacol. 159, 137–157.
Selvamani, S., Balamurugan, S., 2015a. Antibacterial and antifungal activities of different organic solvent extracts of *Acalypha indica* (Linn.). Asian J. Plant Sci. Res. 5, 52–55.
Selvamani, S., Balamurugan, S., 2015b. Phytochemical screening and GC-MS analysis of acetone leaf extract of *Acalypha indica* (Linn.). Int. J. Res. Stud. Biosci. (IJRSB) 3, 4.
Senthilkumar, M., Gurumoorthi, P., Janardhanan, K., 2006. Some medicinal plants used by Irular, the tribal people of Marudhamalai hills, Coimbatore, Tamil Nadu. Nat. Product. Radiance 5, 382–388.
Sharma, J., Gairola, S., Gaur, R., Painuli, R., Siddiqi, T., 2013. Ethnomedicinal plants used for treating epilepsy by indigenous communities of sub-Himalayan region of Uttarakhand, India. J. Ethnopharmacol. 150, 353–370.
Sharma, S., Singh, T., Vijayvergia, R., 2009. Molluscicidal activity of some medicinal plants. J. Herbal. Med. Toxicol. 3, 155–157.
Shirwaikar, A., Rajendran, K., Bodla, R., Kumar, C.D., 2004. Neutralization potential of Viper russelli russelli (Russell's viper) venom by ethanol leaf extract of *Acalypha indica*. J. Ethnopharmacol. 94, 267–273.
Singh, A.G., Kumar, A., Tewari, D.D., 2012. An ethnobotanical survey of medicinal plants used in Terai forest of western Nepal. J. Ethnobiol. Ethnomed. 8, 19.
Sivaraj, R., Rahman, P.K., Rajiv, P., Narendhran, S., Venckatesh, R., 2014. Biosynthesis and characterization of Acalypha indica mediated copper oxide nanoparticles and evaluation of its antimicrobial and anticancer activity. Spectrochim. Acta Part A: Mol. Biomol. Spectrosc. 129, 255–258.
Sivasankari, B., Anandharaj, M., Gunasekaran, P., 2014. An ethnobotanical study of indigenous knowledge on medicinal plants used by the village peoples of Thoppampatti, Dindigul district, Tamilnadu, India. J. Ethnopharmacol. 153, 408–423.
Solomon, R.J., Kallidass, S., Vimalan, J., 2005. Isolation, identification and study of antimicrobial property of a bioactive compound in an Indian medicinal plant *Acalypha indica* (Indian-nettle). World J. Microbiol. Biotechnol. 21, 1231–1236.
Somchit, M., Rashid, R.A., Abdullah, A., Zuraini, A., Zakaria, Z., Sulaiman, M., Arifah, A., Mutalib, A., 2010. In vitro antimicrobial activity of leaves of *Acalypha indica* Linn. (Euphorbiaceae). Afr. J. Microbiol. Res. 4, 2133–2136.
Soruba, E., Sundaram, Vickram, Manian, Ramesh Pathy, Kulanthaivelu, Karikalan, Balasundaram, S., 2015. Antioxidant, antibacterial and anti-inflammatory activity of *Acalypha indica* and *Terminalia chebula*: an in-vitro analysis. Res. J. Pharm. Biol. Chem. Sci. 6, 180.
Steyn, D.G., 1938. The presence of hydrocyanic acid in stock feeds and other plants. J. S. Afr. Vet. Assoc. 9, 60–64.
Stone, B.C., 1970. The flora of Guam. Micronesica, 659.
Sundararaman, P., Djerassi, C., 1977. A convenient synthesis of progesterone from stigmasterol. J. Org. Chem. 42, 3633–3634.
Suri, R., Bakar, H.A., Rehan, A.N., Rosnah, O., Normah, A., 2004. Preliminary studies on the analysis of fatty acids, essential oils and flavonoids in *Acalypha indica* L.. J. Trop. Agric. Food Sci. 32, 163.
Sutriana, A., Aliza, D., Vanda, H., 2010. Aktivitas hepatoprotektif ekstrak etanol daun Kucing-kucingan Acalypha indica L.) pada tikus putih (*Rattus Novergicus*) yang diinduksi parasetamol. J. Ilmu-Ilmu Peternak., 292–298.
Takle, V., Savad, R., Kandalkar, A., Akarte, A., Patel, A., 2011. Pharmacognostic and phytochemical investigations of aerial parts of *Acalypha indica* Linn. Pharmacogn. J. 3, 33–35.
Talapatra, B., Goswami, S., Talapatra, S., 1981. Acalyphamide, a new amide and other chemical-constituents of *Acalypha-indica* Linn. Indian J. Chem. Sect. B-Org. Chem. Incl. Med. Chem. 20, 974–977.
Taufiq-Yap, Y., Peh, T., Hong, P., Ee, G., Rahmani, M., Muse, R., 2000. Insecticidal activity of *Acalypha indica* and *Myristica fragrans*. Trop. Biomed. 17, 93–95.
Taylor, J.C., Rapport, L., Lockwood, G.B., 2003. Octacosanol in human health. Nutrition 19, 192.
The Plant List, 2013. Acalypha indica L., Version 1.1. Available from: ⟨http://www.theplantlist.org⟩. (Accessed 27 February 2017).
Umamaheswari, M., AsokKumar, K., Somasundaram, A., Sivashanmugam, T., Subhadradevi, V., Ravi, T.K., 2007. Xanthine oxidase inhibitory activity of some Indian medical plants. J. Ethnopharmacol. 109, 547–551.
Ved, D.K., Suma, T.S., Vijay, B.V.S., Sathya, S.K., Ravikumar, K.R., Vaibhav, K., Ajith, S., Kumar, S.N., Venugopal, B.S., Somashekhar, M.V., Sumanth, Sugandhi, R., Surekha, K.V., Desale, N., 2016. *Acalypha indica*, FRLHT's ENVIS centre on medicinal plants. Bangalore.
Vimala, S., 2013. Kucing Galak. Institut Penyelidikan Perhutanan Malaysia, Malaysia.
Vogel, H., 2007. Drug Discovery and Evaluation: Pharmacological Assays. Springer Science & Business Media.
Walter, T.M., 2007. Review of *Acalypha indica*. Linn in Traditional Siddha Medicine.
Wang, D., Zhang, S., Chang, Z., Kong, D.-X., Zuo, Z., 2017. Quebrachitol: global status and basic research. Nat. Prod. Bioprospect., 1–10.
Watt, J.M., Breyer-Brandwijk, M.G., 1962. The Medicinal and Poisonous Plants of Southern and Eastern Africa Being an Account of Their Medicinal and Other Uses, Chemical Composition, Pharmacological Effects and Toxicology in Man and Animal.
Wei, J., Kang, L., 2011. Roles of (Z)-3-hexenol in plant-insect interactions. Plant Signal. Behav. 6, 369–371.
Winter, C.A., Risley, E.A., Nuss, G.W., 1962. Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs. Exp. Biol. Med. 111, 544–547.
World Health Organization, 2002. WHO Traditional Medicine Strategy 2002–2005.
World Health Organization, 2017. Tuberculosis.