

A review of two plants used in Bangladesh for toothache and general oral careKhoshnur Jannat¹, Nusratun Nahar², Be-nazir Farzana¹, Rownak Jahan¹, Taufiq Rahman³, Mohammed Rahmatullah^{1*}¹Department of Biotechnology and Genetic Engineering, University of Development Alternative, Lalmatia, Dhaka, Bangladesh²Department of Pharmacy, University of Development Alternative, Lalmatia, Dhaka, Bangladesh³Department of Pharmacology, University of Cambridge, Tennis Court Road, CB2 1PD, UK**Corresponding Author:** Professor Dr. Mohammed Rahmatullah, Dean, Faculty of Life Sciences and Professor, Department of Biotechnology, University of Development Alternative, House 4/4, Block A, Lalmatia, Dhaka-1207, Bangladesh**Type of Publication:** Review Paper**Conflicts of Interest:** Nil**Abstract**

Because of the comparative unhygienic mode of living, which includes not taking proper care of the teeth and gums, toothache and gum diseases are common among the rural and tribal people of Bangladesh. In the absence of qualified dentists and dental diseases' treatment, the people depend on traditional medicinal practitioners like folk and tribal medicinal practitioners, who in turn utilize various medicinal plants for treatment of tooth and gum problems. In this review, we discuss the traditional mode of use of two such plants, namely *Abutilon indicum* and *Acalypha indica*. At the same time, we review comparative ethnic uses in other parts of the world, and discuss the scientific validation of the uses along with potential for discovery of new drugs based on published scientific literature on the phytochemical content and pharmacological properties of the two plants. It is concluded that the two plants merit potential for further scientific research towards discovery of possible novel drugs, which can be effective against tooth and gum disorders.

Keywords: *Abutilon indicum*, *Acalypha indica*, toothache, gum disorders, traditional medicine**Running head:** Plants for toothache and general oral care**Introduction**

Oral diseases can be of many type; among them oral cancer, dental caries, and periodontal diseases constitute the major health problems according to recent reviews and reports [1-3]. A survey of dental health carried out in rural and urban areas of central and western Bangladesh found that except for the 6 year olds, less than 10% in all age groups had a healthy periodontium. In the 18 year olds, shallow pockets were found in 34% of the urban slum group and in 42% of the rural group [4]. Another survey on oral health of 12-year old children found frequent occurrences of poor oral hygiene and bleeding gingiva [5]. In a survey of 6-12 year old children in Bangladesh, it has been found that there is a significant correlation between incidence of dental caries (decayed teeth) and underweight of children [6]. Prevalence of dental caries was associated with lower height, weight and body mass index (BMI) among Bangladeshi children as observed in another

survey ^[7]. Prevalence of gingivitis and plaque accumulation has been observed to be remarkably high among slum dwellers of Bangladesh ^[8].

The scenario presented above for Bangladesh holds true for other countries, especially the under-developed countries. According to the World Health Organization (WHO), in most developing low-income countries, the prevalence of dental caries is high with 90% of the dental caries left untreated. An estimated 5 billion people suffer worldwide from dental caries or tooth decay ^[9]. Dental caries carry a high treatment cost. Although the cost may vary from country to country, just to cite one example, the treatment cost for dental caries for all children below 15 years age in Saudi Arabia (assuming that each child has 6 decayed teeth and the prevalence of dental caries is 84%) comes to 3.9 billion Saudi Riyals (1 Saudi Riyal = 0.27 US\$) ^[10].

The prevalence of dental caries in India is 50-60%. Dental caries is an infectious microbial disease leading to tooth loss and severe pain in the late stages ^[11]. Thus prevention is better than treatment of dental caries. On the other hand, prevention means adoption of good oral hygiene measures necessitating regular brushing of teeth and washing of mouth after consumption of food, especially sweets. People in poor countries, either through lack of knowledge of how to maintain appropriate oral hygiene or because of their inability to purchase toothbrushes and toothpastes or because of absence of quality water fail to observe proper maintenance of their teeth and gums. At the same time, once any dental problem occurs, any proper dentist, doctor and even medicines are either not available or affordable. To get out of this conundrum, people resort to traditional medicinal practitioners, who mostly use plants for both preventive and therapeutic purposes. Notably, the two major things to be used in case of for example occurrence

of dental caries are use of anti-microbial substances and pain alleviating items.

Overview of plants used against dental problems like toothache and bleeding from gums

Plants form an important tool of traditional medicinal practitioners for maintaining oral hygiene and for treatment of various dental problems. In an ethnomedicinal survey carried out in Bargarh district in Odisha State, India, 57 plant species were documented to be used for dental and oral health care. Out of the 57 plant species, 24 were used exclusively for tooth stick, 24 for toothache due to caries, 16 for gum diseases, and 11 for pyorrhea. The Fabaceae and Moraceae families contributed the maximum number of plants with 5 species for each family. Small branches of *Abutilon indicum* were used as tooth brush and leaf paste was used for treatment of toothache. Small branches of *Achyranthes aspera* were also used as tooth brush; twig mixture was used as a wash for tooth pain. Dried root powder was used as tooth paste and for treatment of gum disorders. Cotton soaked in leaf extract was applied to aching tooth and for filling up cavities ^[12].

A review of plants used for oral health care showed that 120 species of plants are used throughout India for maintaining oral health and treatment of oral health disorders ^[13]. It has been shown that a number of plants used for maintenance of oral hygiene contain phytochemicals, which are active against oral bacteria. To cite just one example, the plant *Piper cubeba* contains anti-bacterial components like artocarpesin, macelignan, catechol, and xanthohumol ^[14]. The tribal population of Wayanad district, Kerala, India has been reported to use three plants for teeth cleansing, eight plants as remedy for dental caries or tooth decay, thirteen plants as remedy for toothache, and six plants as treatment for oral ulcers. Among the plants used are roots of *Areca catechu* (for oral

ulcers)^[15]. Traditional healers in Cameroon have been identified to use 52 plants of which 48 are used in the management of toothache, sore throat, mouth sores, abscess, broken tooth and jaw, tooth sensitivity, mouth thrush, dental caries, gingivitis, sinusitis, tonsillitis, xerostomia, oral syphilis, oral cancer, halitosis, and tooth bleaching. Four plants were used for dental extraction^[16]. It may be noted that the majority of the people of Cameroon depend on traditional medicinal practitioners for their health care needs^[17].

An ethnobotanical survey conducted among different tribal communities (Bhills, Gavits, Kokanis, Mavachis, Valvis, Pawras, Koknas, and Vasaves) of Nandurbar district of Maharashtra, India, revealed use of 20 plants for treatment of disorders of oral cavity, particularly tooth decay. The stems of *Achyranthes aspera* were used as tooth brush; ash of the plant was used as tooth powder and to relieve pyorrhea and tooth ache^[18]. Sixty two medicinal plant species have been identified to be used by traditional healers in the Kadiogo Province of Burkina Faso for treatment of mainly gingivitis and toothache^[19].

Seven plant species have been reported to be used in Shamdhara (Oghi), Mansehra, Pakistan for treatment of oral diseases like gum bleeding and toothache^[20]. Eighty seven plant species have been reported to be used in northern India for dental problems with the largest number of plants being used in Himachal Pradesh. Among the various species, *Acalypha indica* whole plant was used for toothache, and leaves and roots of *Achyranthes aspera* were also used for the same purpose^[21]. *A. aspera* was among the 13 plants reported to be used for treatment of dental caries by the Malayali tribals from Kolli Hills, India. Stem of the plant was used as tooth brush. Whole plant ash was used as tooth powder to cure pyorrhea, toothache, and gum bleeding^[22]. The people of Dakshina Kannada, India use 32 plant species to maintain oral

health and hygiene and as remedy for dental diseases. The seeds of Areca catechu are chewed with lime, betel leaf and tobacco to prevent tooth decay^[23].

Streptococcus mutans is the most significant bacteria behind the development of dental caries. Among Indian plant species found to inhibit this bacteria are *Curcuma longa*, *Spilanthes acmella*, *Piper cubeba*, *Morusalba*, *Prosopisspicigera*, *Trachispermum ammi*, *Acacia nilotica*, *Drosera peltata*, *Azadirachta indica*, *Morinda citrifolia*, and *Cocos nucifera*^[24].

A number of plant species are also used by folk and tribal medicinal practitioners in Bangladesh to treat toothache and bleeding from gums. The Soren clan of the Santal tribe residing in Rajshahi district, Bangladesh use roots of *Glycosmis pentaphylla* in combination with garlic (*Allium sativum*) cloves and fruits of black pepper (*Piper nigrum*) for toothache. Stems of *G. pentaphylla* are used for brushing teeth^[25]. Fruits of *Averrhoa carambola* are chewed to obtain relief from toothache by non-Garo folk medicinal practitioners (FMPs), and roots of *Glycosmis pentaphylla* are used by Garo tribal medicinal practitioners (TMPs) for pyorrhea and toothache in Tangail district, Bangladesh^[26]. Stems of *Amaranthus spinosus* are used to brush teeth and gums to alleviate gum bleeds and toothache in Kurigram district, Bangladesh^[27]. Crushed young leaves of *Mangifera indica* are advised to brush teeth to alleviate toothache by FMPs of Narayanganj district, Bangladesh^[28]. The Bede community TMPs of Porabari village, Dhaka district, Bangladesh boils roots of *Mimosa pudica* and advises patients with toothache to gargle with the still warm water^[29]. Paste of root of *M. pudica* is applied to painful tooth as treatment for toothache in Rangpur district, Bangladesh^[30].

In Kishoreganj district, Bangladesh, paste of flowers of *Spilanthes calva* is applied to aching tooth to obtain relief from pain^[31]. Leaves of *S. calva* or *Polygonum*

hydropiper are used for treatment of toothache in Sylhet and Moulvibazar districts, Bangladesh [32]. In a number of ethnomedicinal surveys carried out by us over the last ten years (many of them still not published), it has been observed that more than thirty plant species are used in Bangladesh to treat tooth and gum disorders and oral lesions. The objective of the present report will be to discuss two of these plants used for treatment of toothache or other disorders affecting oral health with regard to their phytochemical constituents and potential for new drug discoveries from these plants. These two plant species are *Abutilon indicum* and *Acalypha indica*. It is obvious that to be good agents for preventing or curing toothache, dental caries or other periodontal diseases, a plant preferably should give both effects, namely anti-bacterial and analgesic as well as be non-toxic and bioavailable.

Abutilon indicum

Analgesic and anti-inflammatory effects of ethanol extract of the plant has been reported for carrageenan-induced hind paw edema model and formalin-induced paw licking and tail flick model in rodents [33]. Methanol extract of whole plant also reportedly gave analgesic activity as determined by Eddy's hot plate method, and anti-inflammatory activity as determined by carrageenan-induced paw edema method in rodents [34].

Phytochemicals isolated from *A. indicum* whole plants include 1-methoxycarbonyl-carboline; 3-hydroxy-damascone; 3-hydroxy-ionol; 3,7-dihydroxychromen-2-one; 4-hydroxyacetophenone; 4-hydroxybenzaldehyde; 4-hydroxybenzoic acid; 4-hydroxybenzoic acid ester; 4-hydroxyphenylacetic acid methyl ester; abutilin A; adenine; adenosine; aurantiamide acetate; benzamide derivative; benzoic acid; coumaric acid; methylindole-3-carboxylate; n-(1-methoxycarbonyl-2'-phenylethyl)-4-hydroxybenzamide; n-feruloyltyrosine; para-coumaric acid; riboflavin; scoparone; scopoletin; sitosterol;

stigmasterol; syringaldehyde; thymine; vanillic acid; vanillin; and (R)-N-(1'-methoxycarbonyl-2'-phenylethyl)-4-hydroxybenzamide [35]. The plant essential oil constituents are mainly, pinene, caryophyllene, caryophyllene oxide, endesmol, farnesol, borneol, geraniol, geranyl acetate, elemene, and cineole [36]. Other compounds reported from the plant include p-hydroxybenzoic acid and sesquiterpene lactones including alantolactone and isoalantolactone [37]. From flowers, the reported compounds include luteolin, chrysoeriol, luteolin 7-O-glucopyranoside, apigenin 7-O-glucopyranoside, quercetin 3-O- β -glucopyranoside, and quercetin 3-O- β -rhamnopyranosyl β -glucopyranoside [38]. Some of the compound structures are shown in Figure 1.

Volatile oil such as eugenol [39], caryophyllene and caryophyllene oxide [40], borneol [41], and geraniol [42] and flavonoids like luteolin, apigenin, and quercetin can act as analgesic and anti-inflammatory agents [43]; from that view point, *A. indicum* has excellent potential to mitigate pain and inflammation from disorders like dental caries. Flavonoids like quercetin inhibit both cyclooxygenase and lipoxygenase activities thus alleviating both pain and inflammation [44].

Ethanol extracts of leaves of *A. indicum* showed anti-bacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Salmonella typhi* [45, 46]. In another study, ethanolic extract of leaves showed anti-bacterial activity against Gram positive organisms like *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina leuka* and *Bacillus megatherium*, and Gram negative organisms like *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Shigella sonnei* [47]. Ethanol extract of whole plant was found to be active against various bacteria species like *Salmonella typhimurium*, *Proteus vulgaris*, *Shigella dysenteriae*, and a fungus, namely *Candida*

albicans [48]. Various solvent extracts of the leaves were found inhibitory against a number of bacterial species like *Bacillus cereus*, *Bacillus megatherium*, *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina lutea*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, *Salmonella typhi*, *Shigella boydii*, *Shigella dysenteriae*, *Vibrio mimicus*, *Vibrio parahemolyticus*, and the fungal species *Candida albicans*, *Aspergillus niger*, and *Saccharomyces cerevisiae* [49].

Ethnomedicinally, the leaves of the plant are used for mouth washes [50]. The root of the plant is also used in ethnic medicine for treatment of gonorrhoea and leprosy, while the fruits are used for coughs and gonorrhoea [51]. The ethnomedicinal uses also point to the anti-bacterial properties of various parts of the plant.

Acalypha indica

Decoction of this herbaceous plant is used for tooth disorders in Tamil Nadu, India [52]. Traditional medicinal practitioners of Khulna City, Bangladesh administer either around 5g of dried plant or 6g of juice obtained from fresh plant for treatment of tooth diseases [53].

Reported bioactive compounds from *A. indica* include 9-tricosene, phytol, dihydroactinidiolide, loliolide, docosanol, 1-eicosanol, 1-triacontanol, 3,7,11,15-tetramethyl-2-hexadecen-1-ol, octacosanol, 5,10-diethoxy-2,3,7,8-tetrahydro-1H,6H-dipyrrolo[1,2-a;1',2'-d]pyrazine, tricosane, 9,12-octadecadienoic acid (Z,Z) methyl ester, hexanedioic acid bis(2-ethylhexyl) ester [54]; the latter compound has anti-bacterial activity [55, 56]. Kaempferol, acalyphine, acalyphamide, 2-methylanthraquinone, tri-O-methyl ellagic acid sitosterol, sitosterol glucoside, stigmasterol, and n-octacosanol have also been reported from the plant [57]. Acalyphine can be used for the treatment of sore gums [58]. Some of the compound structures are shown in Figure 2.

Hexane, chloroform, ethyl acetate and methanol extracts of leaves of *A. indica* reportedly demonstrated inhibitory activities against the Gram-positive microorganisms *Staphylococcus aureus*, *Staphylococcus epidermis*, *Bacillus cereus*, and *Streptococcus faecalis*, and the Gram-negative microorganisms *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus vulgaris*, and *Pseudomonas aeruginosa* [59]. Methanol extract of whole plant showed inhibitory activity against *Salmonella typhimurium*, *Proteus vulgaris*, and *Shigella dysenteriae* and a fungal pathogen, *Candida albicans* [60]. Petroleum ether extract of dried stem, bark and leaves was active against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* [61]. Ethyl acetate and hexane extracts of leaves and roots was found to inhibit the growth of *Bacillus subtilis*, *Staphylococcus aureus* and *Klebsiella pneumonia* [62]. Methanol extract of leaves inhibited the growth of bacteria causing nosocomial infections, the various bacterial species including *Staphylococcus aureus*, *Serratia marcescens*, *Escherichia coli*, *Salmonella typhi*, *Shigella flexneri*, *Klebsiella pneumoniae*, *Vibrio cholerae*, and *Pseudomonas aeruginosa* [63]. Ethanol, methanol, acetone and chloroform extracts of the plant's leaves were active against the bacterial species *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus aureus*, and the fungal species *Candida albicans*, *Aspergillus niger*, *Candida tropicalis* and *Candida kefy* [64]. Water and ethanol extract of the leaves were reportedly more active against the bacterial species *Escherichia coli*, *Salmonella enteritidis*, *Staphylococcus aureus*, and *Bacillus subtilis*, while chloroform extract of the leaves was more active against the fungal species *Candida albicans*, *Candida tropicalis*, *Microsporium canis*, and *Aspergillus fumigatus* [65].

Methanolic extract of *A. indica* showed anti-inflammatory activity in carrageenan-induced rat paw edema and

analgesic activity in acetic acid-induced writhing tests in mice ^[66]. From a number of compounds reportedly present in *A. indica*, namely 2-methylanthraquinone, sitosterol, *n*-octacosanol, and stigmasterol, 2-methylanthraquinone showed best docking score with cyclooxygenase 1 (COX 1) enzyme, which is responsible for synthesis of prostaglandins and causation of pain ^[67]. Sitosterol and stigmasterol are also known for their anti-inflammatory and analgesic properties ^[68, 69]. Thus similar to *A. indicum*, *A. indica* also possess both anti-microbial and analgesic properties, which can be beneficial in alleviating pain and eradication of pathogenic microorganisms involved in oral disorders.

Conclusion

Our comprehensive literature review reveals that both *A. indicum* and *A. indica* have various bioactive phytoconstituents, many of which have been proven to have reported anti-inflammatory, analgesic and anti-bacterial properties. In ethnobotanical uses of extracts derived from these plants, it is likely that multiple constituents contribute to the observed benefits, perhaps with additivity and/or synergy. Future studies may look into concentration response of these known chemicals either single or in combination against suitable models of dental infection and toothache and identification of relevant targets or pathways.

Data availability statement

All data has been cited from published papers which have been abstracted in PubMed, SCOPUS and Google Scholar.

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Conflicts of interest

The authors declare that they do not have any conflicts of interest regarding publication of this paper.

References

1. Torwane NA, Hongal S, Goel P, Chandrashekar BR. Role of Ayurveda in management of oral health. *Pharmacogn Rev* 2014;8:16-21.
2. Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: potential application in the prevention and treatment of oral diseases. *Evid-Based Complement Altern Med* 2011;2011:1.
3. Nagi R. Role of medicinal herbs in management of oral diseases – A review. *IOSR J Dental Med Sci* 2015;14:40-44.
4. Arvidson-Bufano UB, Holm AK. Dental health in urban and rural areas of central and western Bangladesh. *Odontostomatol Trop* 1990;13:81-86.
5. Ullah MS, Aleksejuniene J, Eriksen HM. Oral health of 12-year-old Bangladeshi children. *Acta Odontol Scand* 2002;60:117-122.
6. Mishu MP, Hobdell M, Khan MH, Hubbard RM, Sabbah W. Relationship between Untreated Dental Caries and Weight and Height of 6- to 12-Year-Old Primary School Children in Bangladesh. *Int J Dent* 2013; 2013: Article ID 629675.doi: 10.1155/2013/629675.
7. Mishu MP, Tsakos G, Heilmann A, Watt RG. Dental caries and anthropometric measures in a sample of 5- to 9-year-old children in Dhaka, Bangladesh. *Community Dent Oral Epidemiol* 2018;46:449-456.
8. Hannan MA, Chowdhury MT, Khan MA, Chowdhury AF, Shahidullah KM, Saha AK, Anjum A. Prevalence of Gingivitis, Plaque accumulation and Decayed, Missing and Filled Teeth among slum population in Bangladesh. *Bangladesh Med Res Counc Bull* 2014;40:47-51.
9. World Health Organization (WHO). *Dental Diseases and Oral Health*. WHO, 2003.

10. Marghalani AA, Alshahafi Y, Alshouibi EN. The cost of dental caries in Saudi Arabia. Putting numbers into context. *Saudi Med J* 2014;35:93-94.
11. Shah N. Oral and dental diseases: Causes, prevention and treatment strategies. *NCMH Background Papers – Burden of Disease in India 2003*;pp:275-298.
12. Sahu M, Sahu AR. A preliminary report on the traditional practice for dental and oral health care in Bargarh district of western Odisha, India. *J Med Plants Stud* 2017;5:120-125.
13. Kumar RP. Ethno medicinal plants used for oral health care in India. *Int J Herb Med* 2014;2:81-87.
14. Bairwa R, Gupta P, Gupta VK, Srivastava B. Traditional medicinal plants: Use in oral hygiene. *Int J Pharm Chem Sci* 2012;1:1529-1538.
15. Deepa KC, Jose M, Prabhu V. Ethnomedicinal practices for oral health and hygiene of tribal population of Wayanad, Kerala. *Int J Res Ayur Pharm* 2011;2:1246-1250.
16. Agbor AM, Naidoo S. Ethnomedicinal plants used by traditional healers to treat oral health problems in Cameroon. *Evid-Based Complement Alternat Med* 2015;:Article ID 649832, 2015.
17. Agbor AM, Naidoo S. Knowledge and practice of traditional healers in oral health in the Bui Division, Cameroon. *J Ethnobiol Ethnomed* 2011;7:6.
18. Badgujar SB, Mahajan RT, Kosalge SB. Traditional practice for oral health care in Nandurbar District of Maharashtra, India. *Ethnobot Leaflets* 2008;12:1137-1144.
19. Tapsoba H, Deschamps J-P. Use of medicinal plants for the treatment of oral diseases in Burkina Faso. *J Ethnopharmacol* 2006;104:68-78.
20. Ahmed J, Rahman IU, Shah AH, Farooq M, Khan KR, Ijaz F, Ali N. Some important medicinal plants used for curing dental issues in Shamdhara (Oghi), Mansehra, Pakistan. *EC Dent Sci* 2017;13:3-6.
21. Gupta V, Bansal P, Bansal R, Mittal P, Kumar S. Folklore herbal remedies used in dental care in Northern India and their pharmacological potential. *Am J Ethnomed* 2015;2:365-372.
22. Sekar K, Murugan K, Pandikumar P, Al-Sohaibani S, Ignacimuthu S. Anticaries potential of ethnomedicinal plants used by Malayali tribals from Kolli Hills, India. *Indian J Tradit Knowl* 2016;15:109-115.
23. Jose M, Sharma BB, Shantaram M, Ahmed SA. Ethnomedicinal herbs used in oral health and hygiene in coastal Dakshina Kannada. *J Oral Health Comm Dent* 2011;5:107-111.
24. AdyanathayaA, Ismail S, Sreelakshmi N. Indian traditional medicinal herbs against dental caries – an unsung past to a bright future. *Saudi J Oral Dent Res* 2016;1:1-6.
25. Rahmatullah M, Hasan A, Parvin W, Moniruzzaman M, Khatun A, Khatun Z, Jahan FI, Jahan R. Medicinal plants and formulations used by the Soren clan of the Santal tribe in Rajshahi district, Bangladesh for treatment of various ailments. *Afr J Tradit Complement Alternat Med* 2012;9:350-359.
26. Rahmatullah M, Azam MNK, Rahman MM, Seraj S, Mahal MJ, Mou SM, Nasrin D, Khatun Z, Islam F, Chowdhury MH. A survey of medicinal plants used by Garo and non-Garo traditional medicinal practitioners in two villages of Tangail District, Bangladesh. *Am.-Eur J Sustain Agric* 2011;5:350-357.
27. Das PR, Islam MT, Mahmud ASMSB, Kabir MH, Hasan ME, Khatun Z, Rahman MM, Nurunnabi M, Khatun Z, Lee Y-K, Jahan R, Rahmatullah M. An ethnomedicinal survey conducted among the folk medicinal practitioners of three villages in Kurigram

- district, Bangladesh. Am.-Eur J Sustain Agric 2012;6:85-96.
28. Karim MS, Rahman MM, Shahid SB, Malek I, Rahman MA, Jahan S, Jahan FI, Rahmatullah M. Medicinal plants used by the folk medicinal practitioners of Bangladesh: a randomized survey in a village of Narayanganj district. Am.-Eur J Sustain Agric 2011;5:405-414.
29. Seraj S, Jahan FI, Chowdhury AR, Monjur-E-Khuda M, Khan MSH, Aporna SA, Jahan R, Samarrai W, Islam F, Khatun Z, Rahmatullah M. Tribal formulations for treatment of pain: A study of the Bede community traditional medicinal practitioners of Porabari village in Dhaka district, Bangladesh. Afr J Tradit Complement Alternat Med 2013;10:26-34.
30. Azad AK, Mahmud MR, Parvin A, Chakraborty A, Akter F, Moury SI, Anny IP, Tarannom, SR, Joy SK, Chowdhury SY, Akter S, Rahmatullah M. Medicinal plants of a folk medicinal healer of Rangpur district, Bangladesh. J Med Plants Stud 2014;2:46-50.
31. Sultana T, Akter MN, Papri A, Rahman MA, Shahneowa, AHM, Ashiq AR, Sultana R, Ara I, Islam MT, Das PR, Rahmatullah M. Medicinal plant knowledge of a folk medicinal practitioner of Kishoreganj district, Bangladesh. J Chem Pharm Res 2015;7:732-736.
32. Akter S, Khairuzzaman M, Saleem SM, Sattar F, Rahman I, Yesmin MS, Malek I, Bashir ABMA, Rahmatullah M. Documentation of some folk medicinal practices in Sylhet and Moulvibazar districts, Bangladesh. World J Pharm Pharm Sci 2015;4:176-186.
33. Kumar SS, Marella SS, Vipin S, Sharmistha M. Evaluation of analgesic and anti-inflammatory activity of *Abutilon indicum*. Int J Drug Dev Res 2013;5:99-102.
34. Saraswathi R, Upadhyay L, Venkatakrishnan R, Meera R, Devi P. Phytochemical investigation, analgesic and anti-inflammatory activity of *Abutilon indicum* Linn. Int J Pharm Pharm Sci 2011;3:154-156.
35. Kuo P-C, Yang M-L., Wu P-L, Shih H-N, Thang TD, Dung NX, Wu T-S. Chemical constituents from *Abutilon indicum*. J Asian Nat Prod Res 2008;10:699-703.
36. Patel MK, Rajput AP. Therapeutic significance of *Abutilon indicum*: an overview. Am J PharmTech Res 2013;3:20-35.
37. Sharma PV, Ahmed ZA. Two sesquiterpene lactones from *Abutilon indicum* (Linn.) Sweet. Phytochem 1989;28:3525.
38. Matlawska I, Sikorska M. Flavonoid compounds in the flowers of *Abutilon indicum* (L.) Sweet (Malvaceae). Acta Pol Pharm 2002;59:227-229.
39. Ahmed M, Amin S, Islam M, Takahashi M, Okuyama E, Hossain CF. Analgesic principle from *Abutilon indicum*. Pharmazie 2000;55:314-316.
40. Fidyk K, Fiedorowicz A, Strz̄adala L, Szumny A. □ caryophyllene and □ caryophyllene oxide – natural compounds of anticancer and analgesic properties. Cancer Med 2016;5:3007-3017.
41. Wang S, Zhang D, Hu J, Jia Q, Xu W, Su D, Song H, Xu Z, Cui J, Zhou M, Yang J, Xiao J. A clinical and mechanistic study of topical borneol-induced analgesia. EMBO Mol Med 2017;9:802-815.
42. La Rocca V, da Fonseca DV, Silva-Alves KS, Ferreira-da-Silva FW, de Sousa DP, Santos PL, Quintans-Júnior LJ, Leal-Cardoso JH, de Almeida RN. Geraniol induces antinociceptive effect in mice evaluated in behavioural and electrophysiological models. Basic Clin Pharmacol & Toxicol 2017;120:22-29.

43. Verri Jr WA, Vicentini FTMC, Baracat MM, Georgetti SR, Cardoso RDR, Cunha TM, Ferreira SH, Cunha FQ, Fonseca MJV, Casagrande R. Flavonoids as anti-inflammatory and analgesic drugs: Mechanisms of action and perspectives in the development of pharmaceutical forms. *Stud Nat Prod Chem* 2012;36:297-330.
44. Agrawal AD. Pharmacological activities of flavonoids: A review. *Int J Pharm Sci Nanotechnol* 2011;4:1394-1398.
45. Poonkothai M. Antibacterial activity of leaf extract of *Abutilon indicum*. *Anc Sci Life* 2006;26:39-41.
46. Edupuganti S, Gajula RJ, Kagitha CS, Kazmi N. Antimicrobial activity of *Abutilon indicum*. *World J Pharm Pharm Sci* 2015;4:946-949.
47. Prabahar AE, Thangabalan B, Chavala A, Kumar SS, Kathiravan M, Karthikeyan R. Antibacterial activity of various extracts of *Abutilon indicum* (L.) Sweet leaves. *J Pharm Res* 2009;2:1324-1325.
48. Darsini IP, Shamshad S. Antimicrobial activity and preliminary phytochemical screening of *Abutilon indicum*. *Int J Pharm Biol Sci* 2015;5:6-10.
49. Muhit MA, Sarker AA, Islam MS, Ahmed M. Cytotoxic and antimicrobial activity of the crude extract of *Abutilon indicum*. *Int J Pharmacogn Phytochem Res* 2010;2:1-4.
50. Saini A, Gahlawat DK, Chauhan C, Gulia SK, Ganie SA, Archita, Yadav SS. Ethnomedicinal uses and phytochemistry of *Abutilon indicum* (Linn.) Sweet: an overview. *J Pharmacogn Phytochem* 2015;3:66-72.
51. Kumar VP, Chauhan NS, Padh H, Rajani M. Search for antibacterial and antifungal agents from selected Indian medicinal plants. *J Ethnopharmacol* 2006;107:182-188.
52. Shanmugam S, Gayathri N, Sakthivel B, Ramar S, Rajendran K. Plants used as medicines by Paliyar tribes of Shenbagathope in Virudhunagar District of Tamil Nadu, India. *Ethnobot Leaflets* 2009;13:370-378.
53. Akber M, Seraj S, Islam F, Ferdausi D, Ahmed R, Nasrin D, Nahar N, Ahsan S, Jamal F, Rahmatullah M. A survey of medicinal plants used by the traditional medicinal practitioners of Khulna City, Bangladesh. *Am.-Eur J Sustain Agric* 2011;5:177-195.
54. Chaichoowong S, Bol JB, Bol P, Gamse T, Sriyariyanun M. Chemical profiling of *Acalypha indica* obtained from supercritical carbon dioxide extraction and Soxhlet extraction methods. *Oriental J Chem* 2017;33:66-73.
55. Ge S, Peng W, Li D, Mo B, Zhang M, Qin D. Study on antibacterial molecular drugs in *Eucalyptus granlla* wood extractives by GC-MS. *Pak J Pharm Sci* 2015;28:1445-1448.
56. Peng W, Ge S, Li D, Mo B, Daochun Q, Ohkoshi M. Molecular basis of antibacterial activities in extracts of *Eucommiaul moides* wood. *Pak J Pharm Sci* 2014;27:2133-2138.
57. Selvamani S, Balamurugan S. Phytochemical screening and GC-MS analysis of acetone leaf extract of *Acalypha indica* (Linn.). *Int J Res Stud Biosci* 2015;3:229-232.
58. Hussain AZ, Ignatius A. GC-MS analysis and antimicrobial activity of *Acalypha indica* Linn. *Asian J Chem* 2010;22:3591-3595.
59. Govindarajan M, Jebanesan A, Reetha D, Amsath R, Pushpanathan T, Samidurai K. Antibacterial activity of *Acalypha indica* L. *Eur Rev Med Pharm Sci* 2008;12:299-302.
60. Darsini AIP. Studies on antimicrobial activity of *Acalypha indica* along with preliminary

- phytochemical screening. Int J Life Sci & Pharma Res 2015;5:34-38.
61. Vijayarekha P, Sangottaiyan N, Noorjahan A, Ambiga S. Antibacterial activity of *Acalypha indica* Linn. Int J Curr Microb Appl Sci 2015;4:1133-1138.
62. Gangadevi V, Yogeswari S, Kamalraj S, Rani G, Muthumary J. The antibacterial activity of *Acalypha indica* L. Indian J Sci Technol 2008;1:1-5.
63. Murugan T, Saranraj P. Antibacterial activity of various solvent extracts of the Indian herbal plant *Acalypha indica* against human pathogens causing nosocomial infection. Int J Pharm Biol Arch 2011;2:1473-1478.
64. Chekuri S, Jyoti BA, SompagaS, Panjala S, Anupalli RR. Evaluation of anti microbial and anti fungal activity of *Acalypha indica* L., leaf extract. Int J Pharmacogn Phytochem Res 2018;10:48-51.
65. Somchit MN, Rashid RA, Abdullah A, Zuraini A, Zakaria ZA, Sulaiman MR, Arifah AK, Mutalib AR. *In vitro* antimicrobial activity of leaves of *Acalyphaindica* Linn. (Euphorbiaceae). Afr J Microb Res 2010;4:2133-2136.
66. Rahman MA, Bachar SC, Rahmatullah M. Analgesic and anti-inflammatory activity of methanolic extract of *Acalypha indica* Linn. Pak J Pharm Sci 2010;23:256-258.
67. Mojumdar M, Paul A, Kabir MSH, Rahman MG, Zohora FT, Hasan MS, Ahmed T, Rahman MR, Akter Y, Rahman MM. Molecular docking and pass prediction for analgesic activity of some isolated compounds from *Acalypha indica* L and ADME/T property analysis of the compounds. World J Pharm Res 2016;5:1761-1770.
68. Nirmal SA, Pal SC, Mandal SC, Patil AN. Analgesic and anti-inflammatory activity of stiosrol isolated from *Nyctanthes arbortristis* leaves. Inflammopharmacol 2011;20:219-224.
69. Githinji CG, Mbugua PM, Kanui TI, Kariuki DK. Analgesic and anti-inflammatory activities of 9-hexacosene and stigmaterol isolated from *Mondia whytei*. Phytopharmacol 2012;2:212-223.

Legends Figure

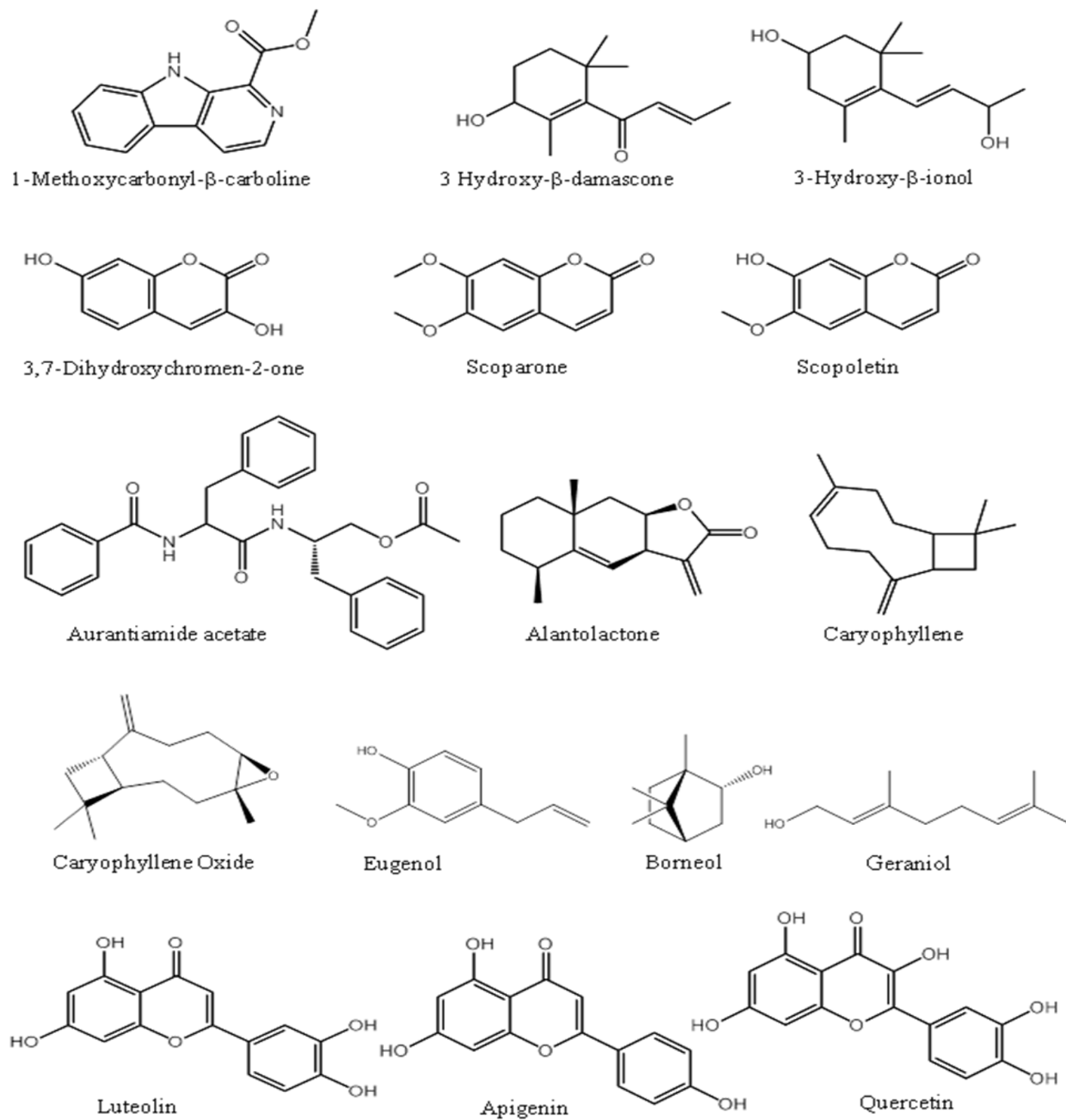


Figure 1. Selected phytochemicals isolated from various parts of *Abutilon indicum*

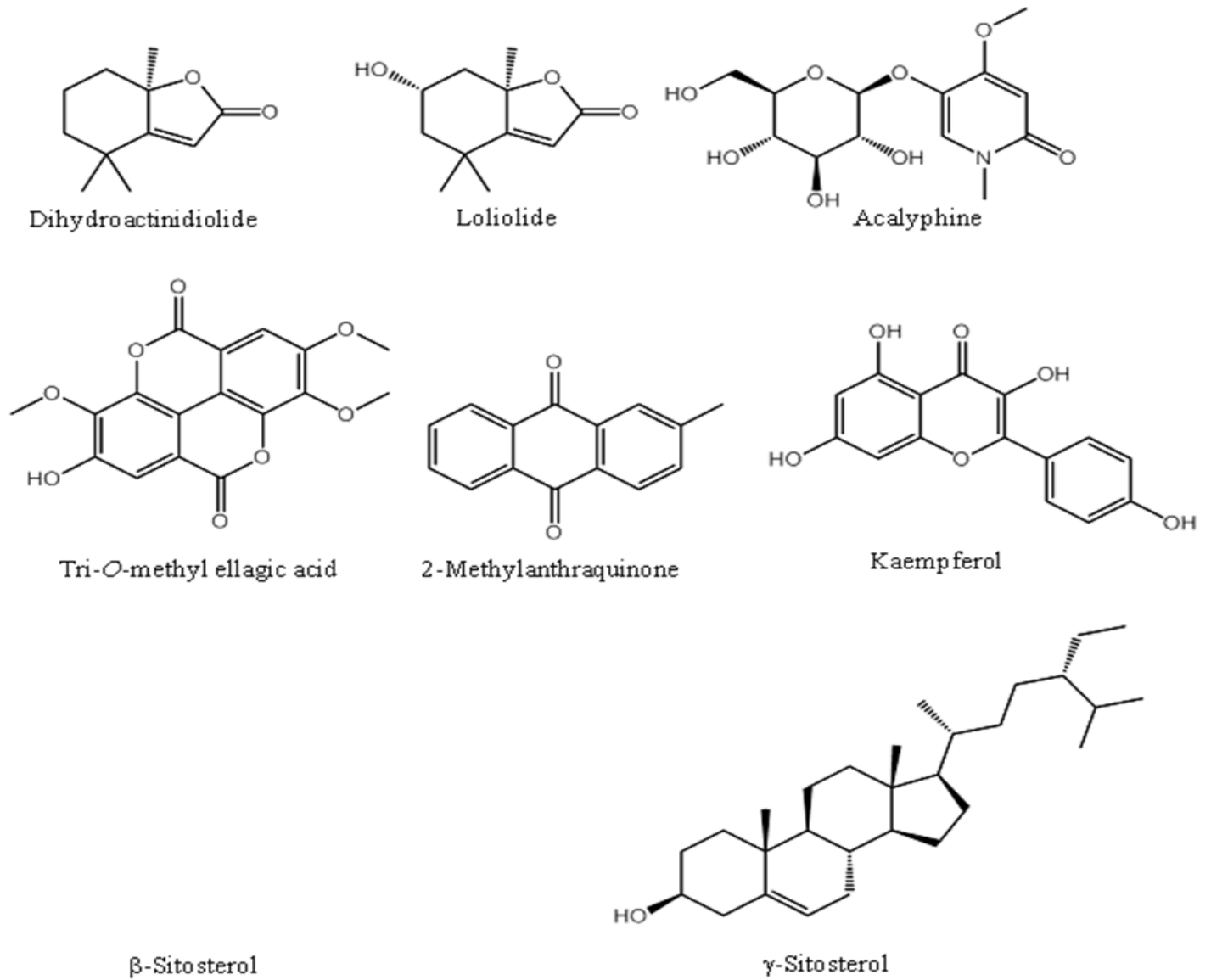


Figure 2. Selected phytochemicals isolated from various parts of *Acalypha indica*