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A review of five traditionally used anti-diabetic plants of Bangladesh and their pharmacological activities

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ABSTRACT

Plants are used traditionally throughout the globe to treat various diseases. Traditionally used medicinal plants are an essential part of the health sector in Bangladesh due to its abundance of a vast source of ethno-medicine. Rural people from developing country like Bangladesh are greatly dependent on traditional source of medicine. The prevalence of diabetes mellitus is increasing from recent years; therefore various researches are going on to discover better medicine to treat this disease. This study has focused on five plants which are *Andrographis paniculata*, *Ageratum conyzoides*, *Swertia chirata*, *Terminalia arjuna*, and *Azadirachta indica* to find out their traditional formulation as anti-diabetic medicine and their pharmacological activity has also been explored through literature search. The available information about traditional anti-diabetic uses of these plants and their pharmacological activities were collected from various electronic sources like Pubmed, SciFinder, Elsevier, Springer, Scopus, Scirus, Science Direct, Google Scholar and Web of Science apart from these locally available books and peer reviewed journal were also used to collect information. This study will help to strengthen the relation between traditional medicine, pharmacology and drug development. A clue may be found from the information provided this review to discover new and better anti-diabetic drugs.

1. Introduction

Ethnobotanical research has been increased recently at greater diversity not only in national level but also at international level. A number of the literature revealed that there is a significant gap exists between scientific validation of ethno-medicine and their uses. Herbal medicines with nutritional value are now a way also used for their pharmacological properties to improve health status [1,2]. Thus plants are used as both food and medicine simultaneously [2,3]. The opportunity of using the plant as a medicine is huge due to the wide diversity of plants around the world. Cultural and geographical factors also facilitated the treatment of various diseases with plants in different formulations like crude extracts, whole plants, a paste of plants, infusions, *etc* [4–6]. Because of producing from natural sources and having less toxic effects, herbal medicines are gaining popularity all over the world [7]. In recent years, a lot of researches revealed that medicinal plants are used to treat diseases in a specific part of the body like the nervous system, cardiovascular systems, respiratory system, digestive and other systems as well as in various organs of the body [8].

Metabolic changes caused by hyperglycemia are called diabetes mellitus and the hyperglycemia may cause due to the defects in insulin action or secretion or in both cases. The available hypoglycemic agents used worldwide such as metformin, sulfonylureas, and glucosidase inhibitors have serious adverse effects such as diabetic ketoacidosis, diarrhea and various diabetes complications [9]. The successful treatment and management of diabetes are yet to be discovered. Within the Indian subcontinent, extensive research has been performed in ethno-medicine system to find out the possible uses of the plant as anti-diabetic agents [10,11].

The fertile Bengal part of the South Asia which got independent in 1971 is called Bangladesh. The country located between latitudes 20° and 27°N, and longitudes 88° and 93°E. This type of location of Bangladesh makes it one of the most fertile countries in the world with alluvial soil. The fertile alluvial soil boasted with a diversified floral source which can be used in different aspects of medicine. Available and smooth nature of traditional herbal medicines made this sector an important part of public health service [12–14]. The geographical

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and cultural similarity of Bangladesh with India influenced the involvement of local people with Indian Ayurveda and Unani medicine.

In the current review article, we have tried to collect information of five plants with hypoglycemic uses in traditional medicine of Bangladesh and their respective pharmacological effects studied through various reputed scientific journals to find out the relation between traditional use and pharmacological effects. This review may also help the scientists and researchers to work in the field of complementary and alternative medicine to find out a possible cure for diabetes and explore the modern health sector. This review also covers the traditional formulations of plants which are used to treat diabetes.

2. Traditional uses as anti-diabetic medicine

After an extensive literature search, it was observed that various parts of the plants are used for the treatment of diabetes and the parts included are leaves, barks, seeds, fruits, stems, flower and in some cases whole plants. Maximum of the plants are used with water and consumed in the early moment of the day. Over the past few decades, a lot of researches have been done about uses and formulation related with diabetes from which we can find out the most common formulations of our featured plants, *i.e.*, *Andrographis paniculata* (*A. paniculata*), *Ageratum conyzoides* (*A. conyzoides*), *Swertia chirata* (*S. chirata*), *Terminalia arjuna* (*T. arjuna*), and *Azadirachta indica* (*A. indica*) [15–18]. Those formulations are given in Table 1.

3. Pharmacological activities

3.1. Pharmacological studies of A. paniculata

3.1.1. Hepato-protective effects

A. paniculata is used in Indian systems of medicine for a long time to treat patients with liver diseases [19]. Not only as a single agent it also used as a component of poly-herbal preparation to treat liver damages [20]. Ram in his studies has observed and reported hepato-protective activity of crude leaves extracts after investigating against CCl_4-induced liver damage [21]. Andrographolide, a compound isolated from *A. paniculata*, has given inhibiting activity against liver injury induced by concanavalin A [22]. Shukla *et al.* has also reported choleretic effects of compound isolated from *A. paniculata* against rats and guinea pigs [23].

3.1.2. Anti-microbial effects

This plant has been investigated for the activity against bacteria, viruses and parasites to find out anti-microbial activity. In a study, daily single dose administration of 0.12–24 g/kg body weight in rats for 6-month durations did not show any anti-bacterial activity [24]. But in another study, alcoholic rhizome extracts showed potential anti-microbial activity against *Ascaris lumbricoides* [25]. Methanolic extracts from *A. paniculata* have also showed significant inhibitory activity against *Plasmodium falciparum* and the concentration needed for 50% inhibition (IC_{50}) value was recorded at 7.2 μg/mL [26].

3.1.3. Hypoglycemic effects

Aqueous *A. paniculata* extract was given potential inhibiting activity to glucose-induced hyperglycemia in normal rabbits and did not show any activity on hyperglycemia induced by epinephrine. Six weeks continuous administrations have no observable effects on blood glucose in fasting condition [27]. But in another study, Subramanian *et al.* stated that *A. paniculata* and andrographolide can produce hypoglycemic effects by inhibiting alpha-amylase and alpha-glucosidase enzymes [28]. A significant anti-diabetic activity was observed in alloxan induced diabetic rats by restoring incapacitated estrous cycle [29].

3.1.4. Anti-oxidant activity

A study done by Trivedi *et al.* suggested that *A. paniculata* plant extracts have potential anti-oxidant activity against y-Glutamyl transpeptidase, glutathione-S-transferase, and lipid peroxidase enzymes with in comparison to Benzenehexa chloride and this study was conducted on mice model [19].

3.1.5. Anti-inflammatory effects

Andrographolide (a compound isolated from *A. paniculata*) and methanolic extract of *A. paniculata* can inhibit lipopolysaccharide-stimulated NO production of macrophage depending on the concentration of the incubated plant sample [30,31]. Another study done by Chiou *et al.* reported that andrographolide can inhibit NO production induced by lipopolysaccharide and can also inhibit inducible nitric oxide synthase production of murine cell line [32].

3.1.6. Effects on cardiovascular disease

Aqueous plant extracts and biologically active compounds isolated from *A. paniculata* have been investigated in animal model to find out significant effects on myocardial infarction. A study has shown that the plant extract from *A. paniculata* can produce hypotensive effects by relaxing the blood vessel so that blood can flow easily to the brain, heart and other parts of the body [33]. Another study suggested that andrographide an active constituent of *A. paniculata* gave a time dependent protection against hypoxia in rat models and this effect was said to be

Table 1
The most common traditional formulations of the featured plants.

Plants name	Family	Bengali name	Formulation used in local areas of Bangladesh
A. paniculata	Acanthaceae	Kalomegh	Usually, the whole plant is used as a drug for treating diabetes. 5 mg Crude paste extract of the whole plant is taken in the morning before breakfast.
A. conyzoides	Asteraceae	Oochunt	Macerated form of the whole plant is taken 1 spoon full twice a day.
S. chirata	Gentianaceae	Chirata	Chirata root is used for the treatment of diabetes with a mixture of honey. It is taken 1–2 g a dose per day in the morning.
T. arjuna	Combretaceae	Arjun	3–6 g per dose of Berks in powder or macerated form with milk is taken 2 h after food.
A. indica	Meliaceae	Neem	The paste of leaf extracts prepared with water is taken at a dose of 2–3 teaspoons daily in empty stomach.

associated with increasing level to cellular glutathione and other anti-oxidant enzymes [34].

3.1.7. Miscellaneous effects

Several studies did in the last 2 decades also suggested its anti-thrombotic, immune-stimulatory, anti-malarial, astringent, anodyne, tonic, alexipharmic and anti-pyretic activities [35]. Not only the plant extracts its compounds like andrographolide, neoandrographolide, dehydroandrographolide, isoandrographolide have also showed various pharmacological activities [36].

3.2. Pharmacological studies of A. conyzoides

3.2.1. Anti-microbial effects

There are various investigations have been conducted to determine the potential anti-microbial activity of *A. conyzoides*. A study has shown that ether and chloroform extract of plant inhibited the growth of *Staphylococcus aureus* [37]. An inhibitory activity of methanolic plant extract against the growth of *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* has been observed by Almagboul *et al.* [38]. The leaf extract was suggested to be active against *Colletotrichum falcatum* and *Rhizoctonia solani* [38].

3.2.2. Analgesic and anti-inflammatory effects

Aqueous extract of *A. conyzoides* leaves at 100–400 mg/kg doses have given significant analgesic activity in rat models [39]. Aqueous extract of leaves was also given to the patients with arthritis and the results revealed that it improved articulation movement towards 24 h of 66% patients without showing any side effect [40]. Another reported study suggested that this plant gave analgesic activity in hot plate method [41]. After treatment for 250 mg/kg hydro alcoholic extracts from a group of rats, the study result suggested that it has significant ($P < 0.05$) anti-inflammatory activity [42].

3.2.3. Wound-healing properties

The excision wound model is usually used to determine wound-healing activities. After treating the model with plant extract and distilled water, it was observed that more than 90% wounds were healed with plant extracts treated group and 72% were healed in the group treated with distilled water [38,43].

3.2.4. Anti-oxidant activity

An ethanol extract of *A. conyzoides* leaves has shown significant activity in DPPH free radical scavenging activity test. The IC_{50} value of plant extract was reported as 18.910 μg/mL and the IC_{50} value of 2.937 μg/mL and 5.100 μg/mL were observed for standard ascorbic acid and butylated hydroxyanisole respectively. The plant extract also showed reducing power and iron chelating activity too [44]. Another study has also reported that Kaempferol (a compound isolated from *A. conyzoides*) gave free radical scavenging activity at (130.07 ± 17.36) g/kg concentration [45].

3.2.5. Anti-diabetic activity

A dose of 500 mg/kg body weight made from aqueous plant extract of *A. conyzoides* reduced fasting blood glucose in an animal model by 39.1%. The study results also suggested that the plant extract possessed lower anti-diabetic activity than the standard anti-diabetic drugs [46]. The results of the study done by Nyunaï *et al.* revealed that that the leaves of *A. conyzoides* can lower the blood glucose levels in normoglycemic and in streptozotocin-induced hyperglycemic rats [47].

3.2.6. Miscellaneous effects

A. conyzoides plant has also possessed some other activities that include spasmolytic effects, gamma radiation effects, anti-cancer and anti-malarial activity [48].

3.3. Pharmacological studies of S. chirata

3.3.1. Hypoglycemic effect

When animal models were treated with a 250 mg/kg *S. chirata* ethanolic plant extract, it significantly reduced the blood glucose level in tolbutamide pretreated, glucose fed and fasted animals [49,50]. Another study reported that albino rat treated with hexane plant extract increased the glycogen content as well as insulin release thus lowered the blood glucose level [51]. Saxena *et al.* reported that Sweechin, a compound of *S. chirata*, enhanced the insulin release from islets in isolated conditions at concentration dependent manner [52].

3.3.2. Hepato-protective activity

A secoiridoids type compound abundant in a butanol fraction of S. chirata has shown significant hepatotoxic activity [53]. A study of Balasundari *et al.* claimed that *S. chirata* leaves extract showed significant *in vivo* hepatoprotective activity [54]. The whole aqueous plant extracts also have shown potent activity in liver disorders [55].

3.3.3. Anti-oxidant activity

Lethal cell injury caused by CCl_4 due to the increasing amount of lipid peroxidation products which can inhibit the anti-oxidant enzyme activity was suggested to being decreased by *S. chirata* plant extract rich in xanthones [54]. These types of anti-oxidant activity can be shown because of radical scavenging activity.

3.3.4. Anti-carcinogenic activity

A study of Banerjee *et al.* suggested that *S. chirata* plant is very rich with xanthones which have potential anti-carcinogenic activity [56]. Aqueous plant extract which is rich with amarogentin have shown anti-carcinogenic activity against mouse skin carcinogenesis induced by dimethyl benzanthracene [57,58].

3.3.5. Anti-inflammatory activity

S. chirata plant is rich in biologically active compound like swerchirin, swertanone and swertianin, and these compounds are active against inflammation [59]. Methanolic and aqueous extracts of whole plants have reported with significant anti-inflammatory activity with increasing dose of administration [60].

3.3.6. Miscellaneous effects

The plant has also been reported to give wound-healing activity [61], anti-pyretic, anthelmintic, anti-periodic, cathartic [62] as well as anti-bacterial activity [63].

3.4. Pharmacological studies of T. arjuna

3.4.1. Cardio-protective effects

Kokkiripati *et al.* reported that *T. arjuna* stem bark has potential cardio-protective activity after analyzing the activity on human monocytic (THP-1) and aortic endothelial cell cultures [64]. *T. arjuna* bark has also shown significant prophylactic activity against catecholamine-induced congestive heart failure [65]. At the dose of 500 mg given to patients having angina showed improved clinical parameters compared to the isosorbidate mononitrate (40 mg/d) standard [66].

3.4.2. Anti-oxidant activity

Dried bark of *T. arjuna* contains lots of anti-oxidant compounds which prevented oxidative stress in rat heart coalition with injured ischemic heart [67]. Another study revealed that arjunolic acid, a compound isolated from *T. arjuna* plant, is found to be active against various oxidative agents like reduced glutathione, lipid peroxidase, DPPH, ascorbic acid and ceruloplasmin [68].

3.4.3. Hypolipidemic activity

A study done by Parmar *et al.* suggested that the bark extract of *T. arjuna* plant can suppress thyroid functions, thus decreasing cardiac and hepatic lipid level in albino rats [69]. Ram *et al.* reported that at the dose of 100 mg/kg ethanolic extract of plant reduced the low density lipoprotein cholesterol level and at the dose of 500 mg/kg the plant extract can also reduce the total cholesterol level [70].

3.4.4. Anti-diabetic activity

An investigation done by Manna *et al.* reported that streptozocin induced (at a dose of 65 mg/kg·body weight) diabetes in albino rat was found to be prevented by arjunolic acid [71]. Injected with streptozocin increased the lipid peroxidations, TNF-α and serum glucose level in injected experimental animals thus induces diabetes [72].

3.4.5. Hypotensive effects

Aqueous and alcoholic extracts of *T. arjuna* bark have showed dose dependent hypotensive effects in experimental animal models [73]. This study also revealed that dog pre-treated with atropine did not show hypotensive effects after treated with alcoholic plant extract, but in another study there was significant hypotensive effects observed after administration of aqueous plant extract of *T. arjuna* [74]. The hypotensive effects of plant extracts in rats were also abolished by pre-treatment with atropine but did not affected by pre-treatment with propranolol [75].

3.4.6. Miscellaneous effects

Arjuna and ellagitanin have possessed and showed significant anti-cancer activity against human breast cancer [76]. *T. arjuna* bark after decoction gave cardio-tonic, diuretic and anti-mutagenic activities [66,77].

3.5. Pharmacological studies of A. indica

3.5.1. Anti-inflammatory and anti-pyretic activity

Carrageenin-induced acute paw edema and formalin-induced arthritis in rats was investigated by administration of nimbidin and sodium nimbidate and the result showed significant anti-inflammatory activity in a dose dependent manner [78,79]. Another study suggested that neem leaf extract has potential anti-inflammatory activity compared to the standard dexamethasone [80] and this activity was shown by suppressing the functions of macrophage and neutrophils [81]. Study results of nimbidin also reported with significant anti-pyretic activity [82].

3.5.2. Anti-diabetic activity

A significant hypoglycemic effect was observed in fasting rabbits after treatment with nimbidin orally [83]. Chloroform extracts of *A. indica* have shown potential reduction of intestinal glucosidase activity and oral glucose tolerance in a murine model [84]. Another study suggested that neem leaves extract possess significant anti-diabetic activity and could use in the treatment of diabetes mellitus [85]. A study done by Kar *et al.* reported that *A. indica* leaf extract have shown significant hypoglycemic activity against alloxan-induced diabetic animal model [50].

3.5.3. Anti-bacterial and anti-viral properties

Bark and leaf extracts of *A. indica* have reported to be effective against bacteria isolated from adult mouth [86] and seed and fruit extracts have shown activity only in higher concentration. The anti-viral activity of *A. indica* was also reported against B Coxsackie viruses [87] and potato virus X [88]. Another study revealed that the methanolic extract of neem acted as a virucidal agent [89].

3.5.4. Hepatoprotective effect

Alcoholic and aqueous leaf extract of *A. indica* exhibited moderate hepato-protective activity against carbon tetrachloride treated animal models [90]. After investigating on rat models, another study suggested that methanolic and aqueous extracts of *A. indica* have possessed significant hepato-protective activity [91]. Aqueous extract of neem was also given a significant protective activity against liver necrosis in rats induced by paracetamol [92].

3.5.5. Effect on central nervous system

Singh *et al.* observed various types of central nervous system depressant activity of *A. indica* leaf extract in mice model [93]. Among other fractions of leaf extracts, acetone fraction showed potential central nervous system depressant activity in mice [94]. At the dose of 200 mg/kg body weight, leaf extract exhibited anxiolytic activity in rats [95].

3.5.6. Miscellaneous effects

Study suggested that ethanolic extract of *A. indica* bark have possessed hypotensive, spasmolytic and diuretic activities [96]. Apart from these activities this plant has also anti-bacterial, anti-malarial, anti-fertility, and anti-oxidant effects [97].

4. Conclusions

After an extensive literature search, all of the plants were found to be effective against diabetes in pharmacological studies in animal models. But this is a matter of question that to what extent these anti-diabetic effects will extrapolate in human settings. To establish these plants as a source of anti-diabetic drugs, extensive chemical investigation as well as clinical trials is needed to find out possible lead compound. Therefore in recent

times, ethno-medicinal sector of medicine has been drawing attention to the researchers to identify plants with anti-diabetic activity which can be useful for mankind.

Conflict of interest statement

The author declares he has no conflict of interest.

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References

[1] Etkin NL, Ross PJ. Food as medicine and medicine as food: an adaptive framework for the interpretation of plant utilization among the Hausa of northern Nigeria. *Soc Sci Med* 1982; **16**(17): 1559-1573.
[2] Totelin L. When foods become remedies in ancient Greece: the curious case of garlic and other substances. *J Ethnopharmacol* 2015; **167**: 30-37.
[3] Towns AM, Van Andel T. Wild plants, pregnancy, and the food-medicine continuum in the southern regions of Ghana and Benin. *J Ethnopharmacol* 2016; **179**: 375-382.
[4] Samuelsson G. *Drugs of natural origin: A textbook of pharmacognosy*. 5th ed. Stockholm: Swedish Pharmaceutical Press; 2004.
[5] Samuelsson G, Bohlin L. *Drugs of natural origin: A textbook of pharmacognosy*. 5th ed. Abingdon: Taylor & Francis; 2004, p. 620-621.
[6] Marques V, Farah A. Chlorogenic acids and related compounds in medicinal plants and infusions. *Food Chem* 2009; **113**(4): 1370-1376.
[7] Mamun-or-Rashid AN, Hossain MS, Naim Hassan B, Kumar Dash M, Sapon A, Sen MK. A review on medicinal plants with antidiabetic activity. *J Pharmacogn Phytochem* 2014; **3**(4): 149-159.
[8] Bailey CJ, Day C. Traditional plants medicines as treatments for diabetes. *Diabetes Care* 1989; **12**(8): 552-556.
[9] Rajalakshmi M, Eliza J, Priya CE, Nirmala A, Daisy P. Antidiabetic properties of *Tinospora cordifolia* stem extracts on streptozotocin-induced diabetic rats. *Afr J Pharm Pharmacol* 2009; **3**(5): 171-180.
[10] Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. *J Ethnopharmacol* 2002; **81**(1): 81-100.
[11] Mukherjee PK, Maiti K, Mukherjee K, Houghton PJ. Leads from Indian medicinal plants with hypoglycemic potentials. *J Ethnopharmacol* 2006; **106**(1): 1-28.
[12] Ashraf A, Chowdhury S, Streefland P. Health, disease and health-care in rural Bangladesh. *Soc Sci Med* 1982; **16**(23): 2041-2054.
[13] Ahmed SM, Hossain MA, Chowdhury MR. Informal sector providers in Bangladesh: how equipped are they to provide rational health care? *Health Policy Plan* 2009; **24**(6): 467-478.
[14] Rahman SA, Kielmann T, McPake B, Normand C. Healthcare-seeking behaviour among the tribal people of Bangladesh: can the current health system really meet their needs? *J Health Popul Nutr* 2012; **30**(3): 353.
[15] Ahmad S. *Lokaj chikitsay vesaja udvid (Traditional treatments and medicinal plants)*. Dhaka: Anupam Prokashni; 2012, p. 1-775.
[16] Alam MJ. *Traditional medicine in Bangladesh*. Dhaka: Asiatic Society of Bangladesh; 2007, p. 1-311.
[17] Ghani A. *Medicinal plants of Bangladesh*. Dhaka: Asiatic Society of Bangladesh; 1998.
[18] Yusuf M, Begum J, Hoque MN, Choudhury JU. *Medicinal plants of Bangladesh—revised and enlarged*. Chittagong: Bangladesh Coun Sci Ind Res Lab; 2009.
[19] Trivedi NP, Rawal UM. Hepatoprotective and antioxidant property of *Andrographis paniculata* (Nees) in BHC induced liver damage in mice. *Indian J Exp Biol* 2001; **39**(1): 41-46.
[20] Rana AC, Avadhoot Y. Hepatoprotective effects of *Andrographis paniculata* against carbon tetrachloride-induced liver damage. *Arch Pharm Res* 1991; **14**(1): 93-95.
[21] Ram VJ. Herbal preparations as a source of hepatoprotective agents. *Drug News Perspect* 2001; **14**(6): 353-363.
[22] Shi G, Zhang Z, Zhang R, Zhang X, Lu Y, Yang J, et al. Protective effect of andrographolide against concanavalin A-induced liver injury. *Naunyn-Schmiedeberg's Arch Pharmacol* 2012; **385**(1): 69-79.
[23] Shukla B, Visen PK, Patnaik GK, Dhawan BN. Choleretic effect of andrographolide in rats and Guinea pigs. *Planta Med* 1992; **58**(2): 146-149.
[24] Leelarasamee A, Trakulsomboon S, Sittisomwong N. Undetectable anti-bacterial activity of *Andrographis paniculata* (Burma) wall. ex ness. *J Med Assoc Thai* 1990; **73**(6): 299-304.
[25] Kaleysa Raj R. Screening of indigenous plants for anthelmintic action against human *Ascaris lumbricoides*: Part I. *Indian J Physiol Pharmacol* 1975; **19**: 47-49.
[26] Mishra K, Dash AP, Swain BK, Dey N. Anti-malarial activities of *Andrographis paniculata* and *Hedyotis corymbosa* extracts and their combination with curcumin. *Malar J* 2009; **8**(1): 26.
[27] Borhanuddin M, Shamsuzzoha M, Hussain AH. Hypoglycaemic effects of *Andrographis paniculata* Nees on non-diabetic rabbits. *Bangladesh Med Res Counc Bull* 1994; **20**(1): 24-26.
[28] Subramanian R, Asmawi MZ, Sadikun A. *In vitro* alpha-glucosidase and alpha-amylase enzyme inhibitory effects of *Andrographis paniculata* extract and andrographolide. *Acta Biochim Pol* 2008; **55**(2): 391-398.
[29] Reyes BA, Bautista ND, Tanquilut NC, Anunciado RV, Leung AB, Sanchez GC, et al. Anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* and their effects on estrous cyclicity of alloxan-induced diabetic rats. *J Ethnopharmacol* 2006; **105**(1): 196-200.
[30] Batkhuu J, Hattori K, Takano F, Fushiya S, Oshiman KI, Fujimiya Y. Suppression of NO production in activated macrophages *in vitro* and *ex vivo* by neoandrographolide isolated from *Andrographis paniculata*. *Biol Pharm Bull* 2002; **25**(9): 1169-1174.
[31] Liu J, Wang ZT, Ji LL, Ge BX. Inhibitory effects of neoandrographolide on nitric oxide and prostaglandin E 2 production in LPS-stimulated murine macrophage. *Mol Cell Biochem* 2007; **298**(1): 49-57.
[32] Chiou WF, Chen CF, Lin JJ. Mechanisms of suppression of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide. *Br J Pharmacol* 2000; **129**(8): 1553-1560.
[33] Huang LY. The effects of andrographolides on experimental blood deficiency of cardiac muscle. *Chin Herb Med* 1987; **18**(7): 26-28.
[34] Woo AY, Waye MM, Tsui SK, Yeung ST, Cheng CH. Andrographolide up-regulates cellular-reduced glutathione level and protects cardiomyocytes against hypoxia/reoxygenation injury. *J Pharmacol Exp Ther* 2008; **325**(1): 226-235.
[35] Prajapati ND, Purohit SS, Sharma AK, Kumar T. *A handbook of medicinal plants, A complete source book*. Jodhpur: Agrobios; 2003, p. 45-46.
[36] Abhishek N, Tewari SK, Alok L. Biological activities of Kalmegh (*Andrographis paniculata* Nees) and its active principles – a review. *Indian J Nat Prod Resour* 2010; **1**(2): 125-135.
[37] Durodola JJ. Antibacterial property of crude extracts from herbal wound healing remedy—*Ageratum conyzoides*. *Planta Med* 1977; **32**(8): 388-390.
[38] Almagboul AZ, Farroq AA, Tyagi BR. Antimicrobial activity of certain Sudanese plants used in folkloric medicine: screening for antibacterial activity, part II. *Fitoterapia* 1985; **56**: 103-109.
[39] Bioka D, Banyikwa FF, Choudhuri MA. Analgesic effects of a crude extract of *Ageratum conyzoides* in the rat. *Acta Hort* 1993; **332**: 171-176.
[40] Marques Neto JF, Costallat LT, Fernandes SR, Napoli MD, Samara AM. Efeitos do *Ageratum conyzoides*, Linèe no tratamento da artrose. *Rev Bras Reumatol* 1988; **28**(4): 109-114.

[41] Abena AA, Kintasngoula-Myaba GS, Diantama J, Bioka D. Effects analgesiques d.un extrait brud. *Ageratum conyzoides* chez le rat. *Encephale* 1993; **19**(4): 329-332.
[42] Shekhar TC, Anju G. A comprehensive review on *Ageratum conyzoides* Linn. (Goat weed). *Int J Pharm Phytopharm Res* 2017; **1**(6): 391-395.
[43] Chah KF, Eze CA, Emuelosi CE, Esimone CO. Antibacterial and wound healing properties of methanolic extracts of some Nigerian medicinal plants. *J Ethnopharmacol* 2006; **104**(1): 164-167.
[44] Hossain H, Karmakar UK, Biswas SK, Shahid-Ud-Daula AF, Jahan IA, Adnan T, et al. Antinociceptive and antioxidant potential of the crude ethanol extract of the leaves of *Ageratum conyzoides* grown in Bangladesh. *Pharm Biol* 2013; **51**(7): 893-898.
[45] Adebayo AH, Tan NH, Akindahunsi AA, Zeng GZ, Zhang YM. Anticancer and antiradical scavenging activity of *Ageratum conyzoides* L. (Asteraceae). *Pharmacogn Mag* 2010; **6**(21): 62.
[46] Agunbiade OS, Ojezele OM, Ojezele JO, Ajayi AY. Hypoglycaemic activity of *Commelina africana* and *Ageratum conyzoides* in relation to their mineral composition. *Afr Health Sci* 2012; **12**(2): 198-203.
[47] Nyunaï N, Njikam N, Abdenneb E, Mbafor J, Lamnaouer D. Hypoglycaemic and antihyperglycaemic activity of *Ageratum conyzoides* L. in rats. *Afr J Trad Compl Alter Med* 2009; **6**(2): 123-130.
[48] Singh SB, Devi WR, Marina A, Devi WI, Swapana N, Singh CB. Ethnobotany, phytochemistry and pharmacology of *Ageratum conyzoides* Linn (Asteraceae). *J Med Plants Res* 2013; **7**(8): 371-385.
[49] Sekar BC, Mukherjee B, Chakravarti RB, Mukherjee SK. Effect of different fractions of *Swertia chirayita* on the blood sugar level of albino rats. *J Ethnopharmacol* 1987; **21**(2): 175-181.
[50] Kar A, Choudhary BK, Bandyopadhyay NG. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. *J Ethnopharmacol* 2003; **84**(1): 105-108.
[51] Chandrasekar B, Bajpai MB, Mukherjee SK. Hypoglycemic activity of *Swertia chirayita* (Roxb ex Flem) Karst. *Indian J Exp Biol* 1990; **28**(7): 616-618.
[52] Saxena AM, Bajpai MB, Murthy PS, Mukherjee SK. Mechanism of blood sugar lowering by a swerchirin-containing hexane fraction (SWI) of *Swertia chirayita*. *Indian J Exp Biol* 1993; **31**(2): 178-181.
[53] Karan M, Vasisht K, Handa SS. Antihepatotoxic activity of *Swertia chirata* on paracetamol and galactosamine induced hepatotoxicity in rats. *Phytother Res* 1999; **13**(2): 95-101.
[54] Balasundari P, Singh SK, Kavimani S. Free radical scavenging of xanthones from *Swertia chirata* Buchham and tumor cell growth inhibition. *Main Group Chem* 2005; **4**(3): 177-185.
[55] Singh HB, Prasad P, Rai LK. Folk medicinal plants in the Sikkim Himalayas of India. *Asian Folk Stud* 2002; **61**: 295-310.
[56] Banerjee S, Sur TK, Mandal SU, Das PC, Sikdar SR. Assessment of the anti-inflammatory effects of *Swertia chirata* in acute and chronic experimental models in male albino rats. *Indian J Pharmacol* 2000; **32**(1): 21-24.
[57] Saha P, Das S. Highlighting the anti-carcinogenic potential of an Ayurvedic medicinal plant, Swertia Chirata. *Asian Pac J Cancer Prev* 2010; **11**(1): 1445-1449.
[58] Saha P, Das S. Regulation of hazardous exposure by protective exposure: modulation of phase II detoxification and lipid peroxidation by *Camellia sinensis* and *Swertia chirata*. *Teratog Carcinog Mutagen* 2003; **23**(S1): 313-322.
[59] Rathore B, Mahdi AA, Paul BN, Saxena PN, Das SK. Indian herbal medicines: possible potent therapeutic agents for rheumatoid arthritis. *J Clin Biochem Nutr* 2007; **41**(1): 12-17.
[60] Mathur A, Verma SK, Singh SK, Mathur D, Prasad GB, Dua VK. Investigation of anti-inflammatory properties of *Swertia chirayta* and *Gloriosa superba*. *Recent Res Sci Technol* 2011; **3**(3): 40-43.
[61] Manjunath KP, Kulkarni GT, Patil KS. Preliminary phytochemical investigation and wound healing activity of the root of *Swertia chirata* Buch. Ham. (gentianaceae). *Indian Drugs* 2006; **43**: 535-537.
[62] Bhargava S, Garg R. Evaluation of antibacterial activity of aqueous extract of *Swertia chirata* Buch. *Ham Root Int J Green Pharm* 2007; **2**: 51-52.
[63] Kirtikar KR, Basu BD. *Indian medicinal plants*. Allahabad: India; 1984, p. 1664-1665.
[64] Kokkiripati PK, Kamsala RV, Bashyam L, Manthapuram N, Bitla P, Peddada V, et al. Stem-bark of *Terminalia arjuna* attenuates human monocytic (THP-1) and aortic endothelial cell activation. *J Ethnopharmacol* 2013; **146**(2): 456-464.
[65] Parveen A, Babbar R, Agarwal S, Kotwani A, Fahim M. Mechanistic clues in the cardioprotective effect of *Terminalia arjuna* bark extract in isoproterenol-induced chronic heart failure in rats. *Cardiovasc Toxicol* 2011; **11**(1): 48-57.
[66] Gauthaman K, Maulik M, Kumari R, Manchanda SC, Dinda AK, Maulik SK. Effect of chronic treatment with bark of *Terminalia arjuna*: a study on the isolated ischemic-reperfused rat heart. *J Ethnopharmacol* 2001; **75**(2): 197-201.
[67] Sumitra M, Manikandan P, Kumar DA, Arutselvan N, Balakrishna K, Manohar BM, et al. Experimental myocardial necrosis in rats: role of arjunolic acid on platelet aggregation, coagulation and antioxidant status. *Mol Cell Biochem* 2001; **224**(1): 135-142.
[68] Parmar HS, Panda S, Jatwa R, Kar A. Cardio-protective role of *Terminalia arjuna* bark extract is possibly mediated through alterations in thyroid hormones. *Pharmazie* 2006; **61**(9): 793-795.
[69] Ram A, Lauria P, Gupta R, Kumar P, Sharma VN. Hypocholesterolaemic effects of *Terminalia arjuna* tree bark. *J Ethnopharmacol* 1997; **55**(3): 165-169.
[70] Manna P, Sinha M, Sil PC. Prophylactic role of arjunolic acid in response to streptozotocin mediated diabetic renal injury: activation of polyol pathway and oxidative stress responsive signaling cascades. *Chem Biol Interact* 2009; **181**(3): 297-308.
[71] Hemalata T, Pulavendram S, Balachandran C, Manohar BM, Puvanakrishnan R. Arjunolic acid: a novel phytomedicine with multifunctional therapeutic applications. *Indian J Exp Biol* 2010; **48**: 238-247.
[72] Singh N, Kapur KK, Singh SP, Shankar K, Sinha JN, Kohli RP. Mechanism of cardiovascular action of *Terminalia arjuna*. *Planta Med* 1982; **45**: 102-104.
[73] Srivastava RD, Dwivedi S, Sreenivasan KK, Chandrashekhar CN. Cardiovascular effects of *Terminalia* species of plants. *Indian Drugs* 1992; **29**: 144-149.
[74] Rose JO, Treadway SC. Herbal support for a healthy cardiovascular system. *Clin Nutr Ins* 1999; **6**: 1-6.
[75] Kandil FE, Nassar MI. A tannin anti-cancer promotor from *Terminalia arjuna*. *Phytochemistry* 1998; **47**(8): 1567-1568.
[76] Bharani A, Ganguli A, Mathur LK, Jamra Y, Raman PG. Efficacy of *Terminalia arjuna* in chronic stable angina: a double-blind, placebo-controlled, crossover study comparing *Terminalia arjuna* with isosorbide mononitrate. *Indian Heart J* 2002; **54**(2): 170-175.
[77] Gupta R, Singhal S, Goyle A, Sharma VN. Antioxidant and hypocholesterolaemic effects of *Terminalia arjuna* tree-bark powder: a randomised placebo-controlled trial. *J Assoc Physicians India* 2001; **49**(1): 231-235.
[78] Bhargava KP, Gupta MB, Gupta GP, Mitra CR. Anti-inflammatory activity of saponins and ot-her natural products. *Indian J Med Res* 1970; **58**(6): 724-730.
[79] Pillai NR, Santhakumari G. Anti-arthritic and anti-inflammatory actions of nimbidin. *Planta Med* 1981; **43**(9): 59-63.
[80] Mosaddek AS, Rashid MM. A comparative study of the anti-inflammatory effect of aqueous extract of neem leaf and dexamethasone. *Bangladesh J Pharmacol* 2008; **3**(1): 44-47.
[81] Kaur G, Sarwar Alam M, Athar M. Nimbidin suppresses functions of macrophages and neutrophils: relevance to its antiinflammatory mechanisms. *Phytother Res* 2004; **18**(5): 419-424.
[82] David SN. Anti-pyretic of neem oil and its constituents. *Mediscope* 1969; **12**: 25-27.
[83] Pillai NR, Santhakumari G. Hypoglycaemic activity of *Melia azadirachta* Linn (neem). *Indian J Med Res* 1981; **74**: 931-933.
[84] Bhat M, Kothiwale SK, Tirmale AR, Bhargava SY, Joshi BN. Antidiabetic properties of *Azardiracta indica* and *Bougainvillea*

spectabilis: in vivo studies in murine diabetes model. *Evid Based Complement Altern Med* 2011; **2011**: 9.

[85] Akter R, Mahabub-Uz-Zaman M, Rahman MS, Khatun MA, Abdullah AM, Ahmed NU, et al. Comparative studies on antidiabetic effect with phytochemical screening of *Azadirachta indicia* and *Andrographis paniculata*. *IOSR J Pharm Biol Sci* 2013; **5**(2): 122-128.

[86] Yerima MB, Jodi SM, Oyinbo K, Maishanu HM, Farouq AA, Junaidu AU, et al. Effect of neem extracts (*Azadirachta indica*) on bacteria isolated from adult mouth. *Nige J Basic Appl Sci* 2012; **20**(1): 64-67.

[87] Badam L, Joshi SP, Bedekar SS. '*In vitro*' antiviral activity of neem (*Azadirachta indica.* A. Juss) leaf extract against group B coxsackieviruses. *J Commun Dis* 1999; **31**(2): 79-90.

[88] Verma VS. Chemical compounds from *Azadirachta indica* as inhibitors of potato virus X. *Acta Microbiol Pol B* 1973; **6**(1): 9-13.

[89] Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and medicinal properties of neem (*Azadirachta indica*). *Curr Sci Bangalore* 2002; **82**(11): 1336-1345.

[90] Kalaivani T, Meignanam E, Premkumar N, Siva R, Vijayakumar V, Rajasekaran C, et al. Studies on hepatoprotective properties of leaf extracts of *Azadirachta indica* A. Juss (Meliaceae). *Ethnobot Leafl* 2009; **13**(2): 165-170.

[91] Devmurari VP, Jivani NP. Hepatoprotective activity of methanolic and aqueous extracts of *Azadirchata indica* leaves. *Int J Pharm-Tech Res* 2010; **2**(2): 1037-1040.

[92] Bhanwra SA, Singh J, Khosla P. Effect of *Azadirachta ondica* (neem) leaf aqueous extract on paracetamol-induced liver damage in rats. *Indian J Physiol Pharmacol* 2000; **44**(1): 64-68.

[93] Singh PP, Junnarkar AY, Reddi GS, Singh KV. *Azadirachta indica*: neuro-psychopharmacological and antimicrobial studies. *Fitoterapia* 1987; **58**: 235-238.

[94] Singh PP, Junnarkar AY, Thomas GP, Tripathi RM, Varma RK. Antidepressant activity of *Azadirachta indica*. *Ibid* 1980; **61**: 164-168.

[95] Jaiswal AK, Bhattacharya SK, Acharya SB. Anxiolytic activity of *Azadirachta indica* leaf extract in rats. *Indian J Exp Biol* 1994; **32**(7): 489-491.

[96] Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Gupta B, Srimal RC. Screening of Indian plants for biological activity: part III. *Ibid* 1971; **9**: 91-102.

[97] Srivastava S, Lal VK, Pant KK. Polyherbal formulations based on Indian medicinal plants as antidiabetic phytotherapeutics. *Phytopharmacology* 2012; **2**(1): 1-5.