Bangladesh Pharmaceutical Journal ***26****(1): 28-35, 2023 (January)*

Stixis suaveolens (Roxb.) Fruit Extract Deciphered Antidepressant and Antidiarrheal Effects via *In vivo* Approach

Md. Monirul Islam[1], Md. Jamal Hossain[1], Miss Sharmin Zahan[1], Farjahan Nur[1], Muhammad Abdullah Al-Mansur[3] and Mohammad A. Rashid[2]

[1]Department of Pharmacy, State University of Bangladesh, 77 Satmasjid Road, Dhanmondi Dhaka-1205, Bangladesh
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka Dhaka-1000, Bangladesh
[3]Institute of National Analytical Research and Service (INARS), Bangladesh Council of Scientific and Industrial Research (BCSIR), Dr. Qudrat-I-Khuda Road, Dhanmondi, Dhaka-1205, Bangladesh

(Received: May 03, 2022; Accepted: September 13, 2022; Published (web): January 31, 2023)

Abstract

Depression is a pervasive psychiatric disorder worldwide and diarrhea is considered a leading cause of preventable death for infants and children in developing countries. The current study was done to assess *in vivo* activities of crude methanol extract of *Stixis suaveolens* fruit, focusing on antidepressant and antidiarrheal effects. The effect on central nervous system (CNS) was examined by recording the onset of sleep and total sleeping time. Besides, castor oil-induced diarrhea in the mice model was followed while evaluating the antidiarrheal effects. Significant ($p<0.01$) reduction in onset time (64.8 min) as well as in total sleeping time (64.8 min) were recorded between the test groups and the control. The extract, when given orally, also resulted in a significant ($p < 0.001$) reduction of diarrheal feces induced by castor oil by 71.43%. The *in vivo* bioassays demonstrated that the crude methanol extract of the fruit of *S. suaveolens* contains significant antidiarrheal and CNS stimulating actions. However, further vigorous studies are recommended to isolate and characterize the major phytoconstituents from the plant in order to develop the exact mechanism of actions of the plant against various disorders.

Key words: *Stixis suaveolens*, diarrhea, depression, traditional uses, methanolic extract.

Introduction

Natural sources, especially plants, herbs and marine lives have been used in medicine since ancient times and are still used today (Sultana *et al*., 2022; Das *et al*., 2022a). Medicinal plants account for 10% of all vascular plants (Fonnegra and Jiménez, 2007), comprising almost half a million species (Pimm *et al*., 2014). When no synthetic medications were available and no idea of surgery existed, the plant kingdom aided greatly in the treatment of ailments (Akinyemi *et al.*, 2018; Alam *et al*., 2022). The usage of these plants has been developed over the generations and this has become known in many contexts as traditional medicine. Many countries in Africa, Asia and Latin America use traditional medicines to meet some of their primary health care needs. Traditional medicine has substantial popularity in all regions of the world. Herbal medicines currently account for business over the 80 billion US Dollers annually and are growing steadily (Idu, 2009). Recently, the number of plant-derived therapeutic approaches, including applications of medicinal plants in nanotechnology have increased globally (Grabley and Sattler, 2003; Salve *et al*., 2022). Nearly 7,000 of the listed medicinal compounds in the Western pharmacopeia are plant-based and according to the World Health Organization (WHO) estimation, 65-80% of the world's population, particularly those who live in vast rural areas of developing countries, rely on herbal medicines as their primary form of healthcare (Ripa *et al*., 2022a; Ripa *et al*., 2022b). Although plant-

Corresponding author: Md. Jamal Hossain, Email: jamal.du.p48@gmail.com; jamalhossain@sub.edu.bd
DOI: https://doi.org/10.3329/bpj.v26i1.64215

derived treatments show promise as therapeutic agents, most plants are not studied for their medicinal potential (Ekor, 2014). As a result, scientific study of medicinal plants' biological activity may aid in justifying their usage in health care (Foye *et al*., 2007).

Traditional medicine is a unique amalgamation of different ethnomedical influences. It includes traditionally entrenched aspects influenced by local indigenous people and close-by Indian Ayurveda and Unani medicine (Bhardwaj and Paul, 1986; Claquin, 1981). Medicinal plants and the use of traditional medicines are an integral part of public health services worldwide, especially in the developing countries (Ashraf *et al*., 1982; Rahman *et al*., 2012). Diarrhea, anxiety and depression disorders are some prevalent diseases. A large number of people get affected by diarrhea in the country each year. With the increasing growth and economic development, anxiety and depression-related issues are increasing worldwide. Medicinal plants could provide effective solutions for these ailments in parallel to the current pharmaceutical options (Mitra *et al*., 2022a; Das *et al*., 2022b).

Diarrhea is a common gastrointestinal condition marked by increased gastrointestinal motility and secretion as well as a decrease in fluid and electrolyte absorption (Bafna and Sarin, 2012; Ezeja *et al*., 2012). In developing countries, it is a significant cause of illness and mortality, mainly affecting neonates and babies (Ezeja *et al*., 2012). It is the second most significant cause of death in children under five, accounting for 370,000 child deaths in 2019 (WHO, 2022; WHO, 2010). 78% of diarrheal deaths of children occur in Africa and Southeast Asia (Browning, 1999; De La Fuente, 2008). Major medications for diarrhea management are antimotility and antisecretory medications, while opioids and their metabolites are still commonly utilized to treat diarrhea.

Anxiety and depression disorders are among the most common psychiatric illnesses today (Griebel and Holmes, 2013; Somers *et al*., 2006). WHO-led studies have identified depression as the second leading cause of disease-related disability by 2020, following heart disease (Lopez and Murray, 1998). The current treatment for depression is generally associated with several adverse side effects, and it is only successful in a small percentage of patients (Nestler *et al*., 2002). For the treatment of depression and anxiety, benzodiazepines and selective serotonin reuptake inhibitors (SSRIs) are generally used (Griebel and Holmes, 2013; Sharp, 2013).

Stixis suaveolens (Roxb.) is a flowering plant in the family Capparaceae. It is distributed in the tropical and sub-tropical regions of southeastern Asia and the Indian subcontinent. It is also available in hilly areas of Bangladesh. This plant is thought to have many biologically active chemicals that could be useful for various medical uses (Su *et al*., 2006). This plant has various uses in traditional medicine, including the use of root, stem bark and leaves to treat painful tendons and bones, rheumatism, eye infections etc. in Vietnam (Anh *et al*., 2019a), use of the fruit for treating cough and malaria by the local population of Nagaland (India), anti-inflammatory and antiarthritic use by indigenous communities in Tripura (Jamir *et al*., 2017; Zhasa *et al*., 2015; Biswas *et al*., 2018) and use of fruits to treat cardiovascular diseases and asthma by local traditional practitioners (Kabirajes) in Bangladesh (Biswas *et al*., 2018). Recently, several phytochemical studies by Anh *et al*. (2020) and Islam *et al*. (2020), has been conducted with the fruit and other extracts of *S. suaveolens* to confirm its pharmacological activity. In this perspective, the present study aims to investigate the antidepressant and antidiarrheal properties of *S. suaveolens* through *in vivo* study.

Materials and Methods

Collection of plant material and preparation of crude extract: The fruits of *S. suaveolens* were collected from the local market. Then the collected sample was dried by sun light for several days and then it was also dried for 24 hours in oven at considerably low temperature (not more than 40^0C). The dried fruits were then ground into coarse powder using high capacity grinding machine. The powdered material (300 gm) was taken in a cleaned, amber color reagent bottle (2.5 L) and soaked in 2.0 L of methanol. The container with its content was sealed by bottle cap and kept for a period of 15 days accompanying occasional shaking and stirring. The whole mixtures were then filtered through a fresh cotton plug and finally with a Whatman No.1 filter paper. The volume of the filtrate was then allowed to evaporate at ambient temperature until approximately 70% solvent was evaporated (Khatun *et al*., 2021; Anjum *et al.*, 2021).

Chemicals: Glibenclamide, phenobarbitone, acetyl salicylic acid and diclofenac sodium were the products of Square Pharmaceutical Ltd., Bangladesh. Morphine injections were purchased from the retail pharmacy of Ganashastha Hospital, Dhanmondi. Folin-Ciocalteu reagent, tert-butyl-1-hydroxytoluene (BHT), methanol, tween-80 and other chemical reagents were the products of Merck specialties, Mumbai. Castor oil was purchased from the local market. All the reagents were ensured to be of analytical grade.

Study design: Swiss albino mice (male) weighing between 25-35 gm and 4-5 weeks old were obtained from Jahangirnagar University. The mice were kept in the animal house of the State University of Bangladesh and fed with standard rodent feed under strictly maintained environment. Environmental changes were carefully monitored and prior to any experiment, the animals were allowed (4 days) to adjust to the new environmental conditions. The Federation of European Laboratory Animal Science Associations (FELASA) guidelines and recommendations were followed to reduce the pain and stress of the experimental mice. For the *in vivo* bioassays, the animals were divided into four groups (Group I, II, III and IV) of 5 individuals. The first two groups (I and II) served as the negative and positive control, whereas group III and IV were fed with 200 and 400 mg/kg body weight (p.o.) of crude extract (Kayser *et al*., 2019).

Data analysis: All the results were recorded in triplicates and results expressed as the mean ± standard error mean (SEM). In order to determine the significance in variables between groups, one-way ANOVA and Post hoc Dunnett's test were performed using SPSS version 25.0 and *p* value less than 0.05 was considered to be statistically significant.

Determination of antidepressant activity: The antidepressant potential of the crude fractions was determined using the phenobarbitone induced sleeping time test according to the works of Herrera-Ruiz *et al*., (2011). The SSCFE at two different doses were fed to the experimental groups followed by intraperitoneal injection of phenobarbitone sodium. All the animals were then monitored to record the time of onset of sleep and total sleeping time for everyone.

Determination of antidiarrheal activity: The anti-diarrheal activity of SSCFE was evaluated using the method of castor oil induced diarrhea in mice (Jannat *et al.,* 2022; Farzana *et al*., 2022). According to this method, each mouse was fed with 1ml of highly pure analytical grade of castor oil which would induce diarrhea. The numbers of fecal stools were recorded for each individual mouse. The observations of the experimental groups were compared against that of the control to evaluate the anti-diarrheal activity of the samples (Saha *et al*., 2012).

Results and Discussion

Effect of S. suaveolens crude extract on the CNS: The oral administration of SSCFE resulted in marked delay in the onset of sleep as well as reduction of duration of sleeping period among the test animals after inducing sedation by phenobarbitone sodium. The extract at 200 and 400 mg/kg caused dose dependent elevation of sleep onset time ($p<0.01$) to 138.2 and 156.4 min, respectively while 91.6 min were recorded in case of control (Figure 1). Similarly, both doses of extract decreased the total sleeping time significantly ($p<0.01$) of 101.8 and 83.6 min respectively whereas the animals in the control group had a sleeping time of 148.4 min (Figure 1).

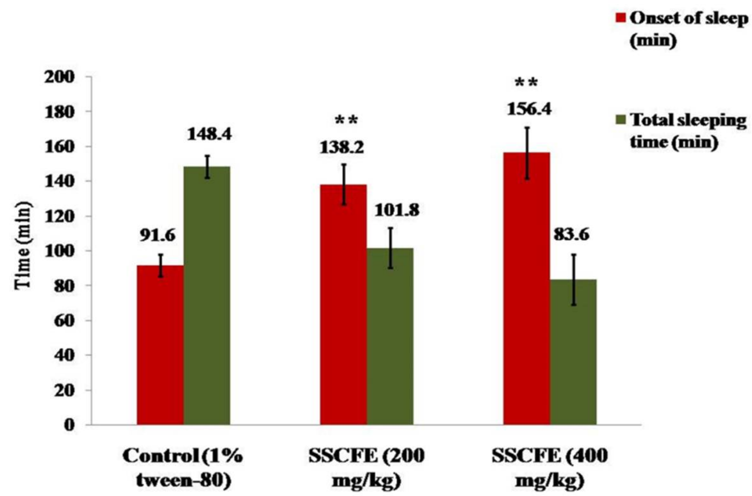

Figure 1. Effect of the oral administration of the SSCFE on the CNS of Swiss albino mice. Here, all the values are expressed as mean ± SEM and SEM = Standard error of mean, SSCFE = *Stixis suaveolens* crude fruit extract. (*) indicates p < 0.05, (**) indicates p<0.05 and (***) indicates p<0.005 compared to the normal group.

CNS stimulants have been suggested to be a viable option for prevention and treatment of depression (Avois *et al.*, 2006). The SSCFE has shown to possess significant amount of CNS activating potential by decreasing both sleeping time interval and sleeping time. Barbiturates like phenobarbitone exhibit their sedative activity by acting on the GABAergic receptors, increasing the influx of chloride ions and inhibition the generation of action potential (Greenfield Jr., 2013). *S. suaveolens* crude extract might possess phytochemicals such as lignans and phenolic compounds, which could inhibit the action of barbiturates (Anh *et al.*, 2019a; Anh *et al.*, 2019b). There have been records of molecules derived from plants i.e., bicuculline and picrotoxin which are strong GABA antagonists capable of reversing the effect of phenobarbitone (Akhter *et al.*, 2021).

As numerous drugs could be linked back to plant origin, similarly the current available CNS-active agents i.e., stimulants are mostly derived from plants (Mitra *et al.*, 2022b). Therefore, there is a huge possibility of finding new phytochemicals with CNS stimulant or anti-depressant activity with better efficacy from the plant (Anh *et al.*, 2019a; Anh *et al.*, 2019b).

Antidiarrheal activity of S. suaveolens crude extract: The crude methanol extract of *S. suaveolens* exhibited significant reduction of average diarrheal feces at a dose of 400 mg/kg (p < 0.01) and the results were comparable to the standard antidiarrheal drug loperamide (2 mg/kg orally). The number of diarrheal feces after 4 hours of the oral treatment were found to be 9.33 ± 0.24, 3.33 ± 0.24, 5.67 ± 0.47, 2.67 ± 0.24 for the group I (normal control), group II (standard loperamide or positive control), group III (200mg/kg b.w.) and group IV (400mg/kg b.w.), respectively (Figure 2).

The antidiarrheal activity of SSCFE has been reported for the first time in this study. This activity is an indication of its use in various stomach associated disorders like cramps, constipation, indigestions etc. One of the various mechanisms by which castor oil induces diarrhea is electrolyte permeability via endogenous prostaglandin secretion (Anjum *et al.*, 2022; Farzana *et al.*, 2022; Jannat *et al.*, 2022). One of the potential reasons by which the SSCF shows its antidiarrheal activity by inhibiting prostaglandin synthesis in the intestine is evident by the fact that the feces after treatment were rather dry (Bahekar and Kale, 2015).

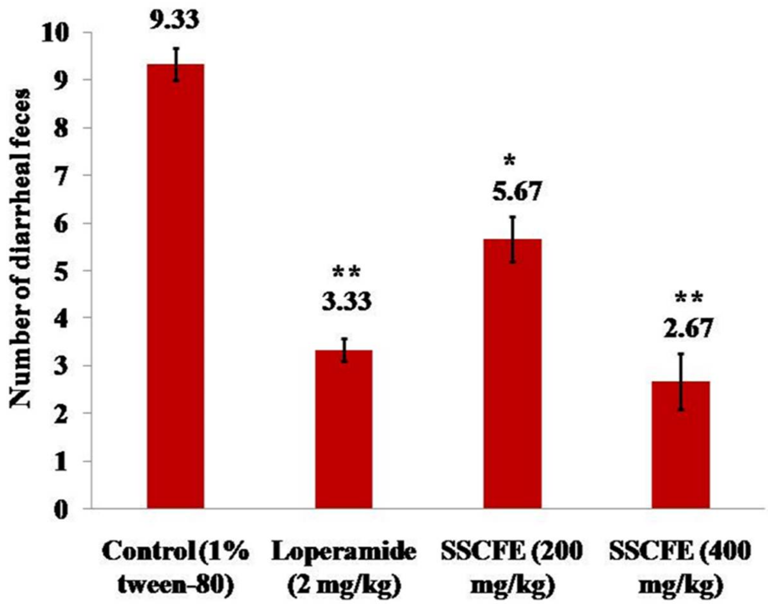

Figure 2. Effect of the oral administration of the SSCFE on the castor oil induced diarrhea in Swiss albino mice. Here, all values are expressed as mean ± SEM and SEM = Standard error of mean, SSCFE = *S. suaveolens* crude fruit extract. (*) indicates $p < 0.05$, (**) indicates $p < 0.05$ and (***) indicates $p < 0.005$ compared to the normal control group.

Conclusion

The present *in vivo* biological studies, for the first-time reports that the crude fruit extract of *S. suaveolens* possess phytoconstituents capable of inducing significant CNS stimulant and antidiarrheal properties. Besides, the crude methanolic extract of its fruit have been found to be safe and induced no side effects at a maximum dose of 400 mg/kg b.w. in Swiss albino mice. This study will evoke future phytochemical research in order to isolate and characterize the bioactive molecules responsible for the CNS stimulant and antidiarrheal activity. Hence, further extensive studies on isolation of the phytoconstituents and investigation on clinical level could lead to the discovery and development of new therapeutic entities from the plant.

Acknowledgement

The authors are grateful to the Department of Pharmacy, State University of Bangladesh, Dhaka, Bangladesh, for providing necessary instrumental and laboratory supports.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

None to declare.

References

Akhter, S., Begum, S., Hasan, M., Kobir, M.E., Khanom, A., Islam, M.J., Hossain, M.S., Das, P., Islam, M.T., Yasmin, M.N. and Rahman, M.M. 2021. A pharmacological study on *Stixis suaveolens* (Roxb.) using experimental animal model. *Discover. Phytomed.* **8**, 10-14.

Akinyemi, O., Oyewole, S. O., and Jimoh, K. A. 2018. Medicinal plants and sustainable human health: a review. *Hort. Int. J.* **2**, 194-195.

Alam, S., Dhar, A., Hasan, M., Richi, F.T., Emon, N.U., Aziz, M., Mamun, A.A., Chowdhury, M., Rahman, N., Hossain, M.J. and Kim, J.K. 2022. Antidiabetic potential of commonly available fruit plants in Bangladesh: updates on prospective phytochemicals and their reported MoAs. *Molecules* **27**, 8709.

Anh, N.Q., Yen, T.T., Hang, N.T., Anh, D.H., Viet, P.H., Hoang, N.H., Van Doan, V. and Van Kiem, P. 2019a. Lignan compounds from *Stixis suaveolens*. *Vietnam J. Chem.* **57**, 304-310.

Anh, N.Q., Yen, T.T., Hang, N.T., Anh, D.H., Viet, P.H., Hoang, N.H., Van Doan, V. and Van Kiem, P. 2019b. Phenolic and lignan compounds from *Stixis suaveolens*. *Vietnam J. Chem.* **57**, 311-317.

Anh, N.Q., Thanh, H.D., Yen, T.T., Anh, D.H., Schmitz Oliver, J. and Viet, P.H. 2020. Characterization of volatile components from ethyl acetate extract of *Stixis suaveolens* (Roxb.) by comprehensive two-dimensional gas chromatography hyphenated with a time of flight mass spectrometer. *Vietnam J. Chem.* **58**, 261-266.

Anjum, N., Hossain, M.J., Haque, M.R., Chowdhury, A., Rashid, M.A. and Kuddus, M.R. 2021. Phytochemical investigation of *Schleichera oleosa* (Lour.) Oken Leaf. *Bangladesh Pharm. J.* **24**, 33-36.

Anjum, N., Hossain, M.J., Aktar, F., Haque, M.R., Rashid, M.A. and Kuddus, M.R. 2022. Potential *in vitro* and *in vivo* bioactivities of *Schleichera oleosa* (lour.) oken: a traditionally important medicinal plant of Bangladesh. *Res. J. Pharm. Technol.* **15**, 113-121.

Ashraf, A., Chowdhury, S. and Streefland, P. 1982. Health, disease and health-care in rural Bangladesh. *Soc. Sci. Med.* **16**, 2041-2054.

Avois, L., Robinson, N., Saudan, C., Baume, N., Mangin, P. and Saugy, M. 2006. Central nervous system stimulants and sport practice. *British J. Sports Med.* **40**, i16-i20.

Bafna, P.A. and Sarin, R.V. 2012. Herbal antidiarrheals: a review. *Int. J. Res. Pharm. Biomed. Sci.* **3**, 637-649.

Bahekar, S.E. and Kale, R.S., 2015. Antidiarrheal activity of ethanolic extract of *Manihot esculenta* Crantz leaves in Wistar rats. *J. Ayurved. Integrat. Med.* **6**, 35-40.

Bhardwaj, S.M. and Paul, B.K. 1986. Medical pluralism and infant mortality in a rural area of Bangladesh. *Soc. Sci. Med.* **23**, 1003–1010.

Biswas, S.C., Majumdar, M., Das, S. and Misra, T.K. 2018. Diversity of wild edible minor fruits used by the ethnic communities of Tripura, India. *Indian J. Tradit. Knowl*. **17**, 282-289.

Browning, S.M. 1999. Constipation, diarrhea and irritable bowel syndrome. *Primary Care* **26**, 113-139.

Claquin, P. 1981. Private health care providers in rural Bangladesh. *Soc. Sci. Med. Med. Anthropol.* **15**, 153-157.

Das, R., Rauf, A., Mitra, S., Emran, T.B., Hossain, M.J., Khan, Z., Naz, S., Ahmad, B., Meyyazhagan, A., Pushparaj, K. and Wan, C.C. 2022a. Therapeutic potential of marine macrolides: an overview from 1990 to 2022. *Chemico-Biological Interact.* **365**, 110072.

Das, R., Mitra, S., Tareq, A.M., Emran, T.B., Hossain, M.J., Alqahtani, A.M., Alghazwani, Y., Dhama, K. and Simal-Gandara, J. 2022b. Medicinal plants used against hepatic disorders in Bangladesh: a comprehensive review. *J. Ethnopharmacol.* **282**, 114588.

De La Fuente, R., Namkung, W., Mills, A. and Verkman, A.S. 2008. Small-molecule screen identifies inhibitors of a human intestinal calcium-activated chloride channel. *Mol. Pharmacol.* **73**, 758-768.

Ekor, M. 2014. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front. Pharmacol.* **4**, 177.

Ezeja, I.M., Ezeigbo, I.I., Madubuike, K.G., Udeh, N.E., Ukweni, I.A., Akomas, S.C. and Ifenkwe, D.C. 2012. Antidiarrheal activity of *Pterocarpus erinaceus* methanol leaf extract in experimentally-induced diarrhea. *Asian Pacific J. Trop. Med.* **5**, 147-150.

Farzana, M., Hossain, M.J., El-Shehawi, A.M., Sikder, M.A.A., Rahman, M.S., Al-Mansur, M.A., Albogami, S., Elseehy, M.M., Roy, A., Uddin, M.A. and Rashid, M.A. 2022. Phenolic constituents from *Wendlandia tinctoria* var. *grandis* (Roxb.) DC. stem deciphering pharmacological potentials against oxidation, hyperglycemia and diarrhea: phyto-pharmacological and computational approaches. *Molecules* **27**, 5957.

Fonnegra, G. R. and Jiménez, R. S. L. 2007. Plantas Medicinales Aprobadasen Colombia. Editorial Universidad de Antioquia, Medellín, Colombia.

Foye, W.O., Majhenič, L., Škerget, M. and Knez, Ž. 2007. Antioxidant and antimicrobial activity of *guarana* seed extracts. *Food Chem.* **104**, 1258-1268.

Grabley, S. and Sattler, I. 2003. Natural products for lead identification: nature is a valuable resource for providing tools. *Modern Meth. Drug Discover*. **93**, 87-107.

Greenfield Jr, L.J. 2013. Molecular mechanisms of antiseizure drug activity at $GABA_A$ receptors. *Seizure* **22**, 589-600.

Griebel, G. and Holmes, A. 2013. 50 years of hurdles and hope in anxiolytic drug discovery. *Nat. Rev. Drug. Discov.* **12**, 667-687.

Herrera-Ruiz, M., Zamilpa, A., González-Cortazar, M., Reyes-Chilpa, R., León, E., García, M.P., Tortoriello, J. and Huerta-Reyes, M. 2011. Antidepressant effect and pharmacological evaluation of standardized extract of flavonoids from *Byrsonima crassifolia*. *Phytomedicine* **18**, 1255-1261.

Idu, M. 2009. The plant called medicine: The 104th Inaugural Lecture Series of University of Benin City, Nigeria.

Islam, M.M., Ahmed, T., Khatun, H. and Rashid, M.A. 2020. Bioactivities of *Stixis suaveolens* (Roxb.) fruit extract: an evaluation in mice model. *Bangladesh Pharm. J.* **23**, 135-140.

Jamir, H. and Tsurho, K. 2017. Documentation of medicinal plants and its uses by Phom tribe of Longleng district, Nagaland. *J. Med. Plants Stud.* **5**, 170-174.

Jannat, T., Hossain, M.J., El-Shehawi, A.M., Kuddus, M.R., Rashid, M.A., Albogami, S., Jafri, I., El-Shazly, M. and Haque, M.R. 2022. Chemical and pharmacological profiling of *Wrightia coccinea* (Roxb. Ex Hornem.) sims focusing antioxidant, cytotoxic, antidiarrheal, hypoglycemic and analgesic properties. *Molecules* **27**, 4024.

Kayser, M.S., Bashar, M.B., Ahmed, T. and Al Aman, D.A. 2019. *In vivo* anti-diarrheal and CNS depressant activities of *Hemigraphis hirta* (Vahl) T. Anders. *Bangladesh Pharm. J.* **22**, 176-180.

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A. and Rahman, S.A. 2021. Isolation of phytochemical constituents from *Stevia rebaudiana* (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via *in vitro* and *in silico* approaches. *Heliyon* **7**, e08475.

Lopez, A.D. and Murray, C.J. 1998. The global burden of disease, 1990–2020. *Nature Med*. **4**, 1241-1243.

Mitra, S., Lami, M.S., Uddin, T.M., Das, R., Islam, F., Anjum, J., Hossain, M.J. and Emran, T.B. 2022a. Prospective multifunctional roles and pharmacological potential of dietary flavonoid narirutin. *Biomed. Pharmacother.* **150**, 112932.

Mitra, S., Muni, M., Shawon, N.J., Das, R., Emran, T.B., Sharma, R., Chandran, D., Islam, F., Hossain, M.J, Safi, S.Z. and Sweilam, S.H. 2022b. Tacrine derivatives in neurological disorders: focus on molecular mechanisms and neurotherapeutic potential. *Oxid. Med. Cell. Longev*. **2022**, Article ID 7252882.

Nestler, E.J., Barrot, M., DiLeone, R.J., Eisch, A.J., Gold, S.J. and Monteggia, L.M. 2002. Neurobiology of depression. *Neuron* **34**, 13-25.

Pimm S. L., Jenkins C. N., Abell R., Brooks T. M., Gittleman J. L., Joppa L. N., Raven P. H., Roberts C. M. and Sexton J. O. 2014. The biodiversity of species and their rates of extinction, distribution and protection. *Science* **344**, 1246752.

Ripa, F.A., Hossain, M.J., Nesa, M.L., Zahan, M.S., Mitra, S., Rashid, M.A., Roy, A., Alghamdi, S., Almehmadi, M. and Abdulaziz, O. 2022a. Phytochemical and pharmacological profiling of *Heritiera fomes* Buch. Ham. deciphered thrombolytic, antiarthritic, anthelmintic, and insecticidal potentialities via *in vitro* approach. *Evid-Based Complement. Alternat. Med.* **2022,** Article ID 2594127.

Ripa, F.A., Hossain, M.J., Munira, M.S., Roy, A., Riya, F.H., Alam, F., Feda, F.B., Taslim, U., Nesa, M.L., Rashid, M.A. and Khidir, E.B. 2022b. Phytochemical and pharmacological profiling of *Trewia nudiflora* Linn. leaf extract deciphers therapeutic potentials against thrombosis, arthritis, helminths and insects. *Open Chem.* **20**, 1304-1312.

Rahman, S.A., Kielmann, T., McPake, B. and Normand, C. 2012. Healthcare-seeking behaviour among the tribal people of Bangladesh: can the current health system really meet their needs? *J. Health Popul. Nutr.* **30**, 353-365.

Saha D. and Paul S. 2012. Study of antidiarrhoeal activity of two Bangladeshi medicinal plants in castor-oil induced diarrhoea. *Res. J. Pharm. Technol.* **5**, 800-804.

Salve, P., Vinchurkar, A., Raut, R., Chondekar, R., Lakkakula, J., Roy, A., Hossain, M.J., Alghamdi, S., Almehmadi, M., Abdulaziz, O. and Azlina, M.F.N. 2022. An evaluation of antimicrobial, anticancer, anti-inflammatory and antioxidant activities of silver nanoparticles synthesized from leaf extract of *Madhuca longifolia* utilizing quantitative and qualitative Methods. *Molecules* **27**, 6404.

Sharp, T. 2013. Molecular and cellular mechanisms of antidepressant action. *Curr. Top. Behav. Neurosci.* **14**, 309-325.

Somers, J.M., Goldner, E.M., Waraich, P. and Hsu, L. 2006. Prevalence and incidence studies of anxiety disorders: a systematic review of the literature. *Can. J. Psychiatr.* **51**, 100-113.

Su, J.X., Wang, W., Zhang, L.B. and Chen, Z.D. 2006. Phylogenetic placement of two enigmaticgenera, *Borthwickia* and *Stixis*, based on molecular and pollen data and the description of a new family of Brassicales, Borthwickiaceae. *Taxon* **61**, 601-611.

Sultana, A., Hossain, M.J., Kuddus, M.R., Rashid, M.A., Zahan, M.S., Mitra, S., Roy, A., Alam, S., Sarker, M.M.R. and Naina Mohamed, I. 2022. Ethnobotanical uses, phytochemistry, toxicology, and pharmacological properties of *Euphorbia neriifolia* Linn. against infectious diseases: a comprehensive review. *Molecules* **27**, 4374.

WHO. 2010. Integrated Management of Childhood Illness, Departments of Child and Adolescent Health and Development and HIV/AIDS. Available from: https://www.who.int/teams/maternal-newborn-child-adolescent-health-and-ageing/child-health/integrated-management-of-childhood-illness/ (Accessed December 1, 2022)

WHO. 2022. Diarrhoea. Available from https://www. who.int/health-topics/diarrhoea#tab =tab_1 (Accessed June 11, 2022)

Zhasa, N.N., Hazarika, P.T.Y., Zhasa, N.N., Hazarika, P. and Tripathi, Y.C. 2015. Indigenousknowledge on utilization of plant biodiversity for treatment and cure of diseases of human beings in Nagaland, India, a case study. *Int. Res. J. Biol. Sci.* **4**, 89-106.