Review Article

Medicinal Plants: Nature's Prodigy for Hyperuricemia and its related Upshot

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Abstract

Uric acid formation occurs both endogenously and exogenously in the liver, intestines, and blood vessel endothelium when injured, dying, and dead cells transform the nucleic acids adenine and guanine into uric acid. Atypically high levels of uric acid in the blood, or Hyperuricemia, can cause gout and arthritis. Over the past few years, hyperuricemia has become increasingly prevalent. Various studies reported that the increased level of uric acid in blood is not only associated with gout but also may contributory factor for cardiovascular diseases such as hypertension, atrial fibrillation, chronic kidney disease, heart failure, coronary artery disease, and cardiovascular death. There has been an emergent attention in uric acid because of the increased prevalence of hyperuricemia worldwide and its induced metabolic disorders. This review article summarizes various traditional plants and their chemical constituents utilized in the cure and treatment of elevated levels of uric acid and its repairable risk factors.

Key words: Hyperuricemia, Metabolic disorder, Uric acid.

Introduction

The production and metabolism of uric acid are complex processes comprising by various factors as regulating hepatic production including renal and gut excretion of this complex [1].Uric acid consists of $C_5H_4N_4O_3$, 7, 9-dihydro-1H-purine-2, 6, 8(3H)-trione that under physiological conditions can easily be converted to the corresponding urate [2-3].Uric acid represents the end-product of purine metabolism in humans, which is mainly regulated by xanthine oxidoreducatase[4].Different organs and tissues can produce uric acid such as intestines, liver, kidneys, muscles, vascular endothelium, and even apoptic cell [5]. Uric acid is either produced when the body breaks purine occurred naturally or supplied from certain foods. Consequently, some animal and plant foods with high purine contents should be avoided from diet especially in persons suffer from gout, as the overproduction of uric acid can induce Hyperuricemia which is linked to gout.

During this process, living and dying cells break down their nucleic acids, adenine and guanine into uric acid. Adenine and guanine are transformed into inosine and guanosine, respectively, by deamination and dephosphorylation. Inosine and guanosine are transformed to hypoxanthine and guanine, respectively, by the enzyme purine nucleoside phosphorylase. These purine bases are then both converted to xanthine by xanthine oxidase, oxidation of hypoxanthine and deamination of guanine by guanine deaminase. Xanthine is further oxidized by xanthine oxidase to uric acid[2]. The production and catabolism of purines are relatively constant between 300 and 400 mg per day. The kidneys eliminate approximately two-thirds, while the gastrointestinal tract eliminates one third of the uric acid load. Almost all uric acid is filtered from glomeruli, while post glomerular reabsorption and secretion regulate the amount of uric acid excretion. The proximal tubule is the site uric acid reabsorption and secretion, and approximately 90% is reabsorbed into blood.

In many mammals, uric acid is further degraded to allantoin by uricase and eventually to ammonia by ureas, but the lack of urease in humans results in uric acid levels at the theoretical limit of solubility in the serum (6.8mg/dl)[6].A healthy body maintains a balance between Uric acid synthesis and excretion. If this is imbalanced it occurs to Hyperuricemia. Hyperuricemia will be occur if Uric acid levels more than 7 mg/dl in male or UA levels more than 6 mg/dl in female[7]. Arthritis and rheumatic pain are brought through the formation of uric acid and urate in the form of calculi in the joints and/or connective tissues. They may also deposit in kidneys induced by and/or ureters causing kidney disease or failure· When high fructose intake occurs, fructose phosphorylation into fructose 1-phosphate is fast, but the reaction with aldolase is slow.

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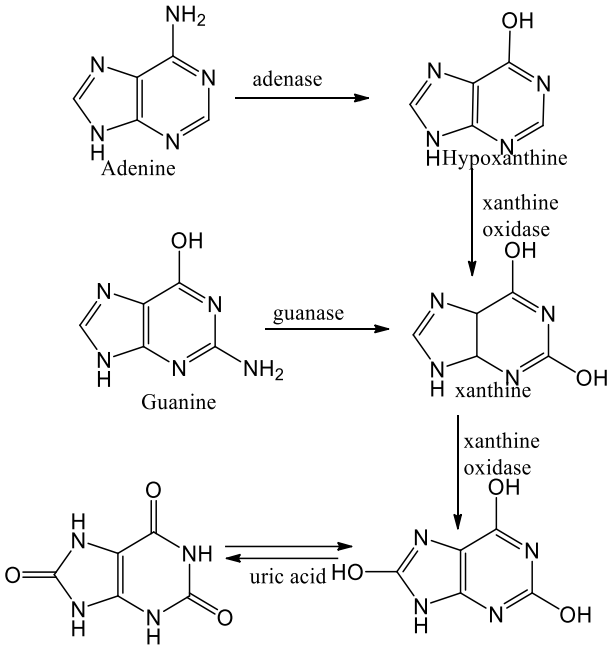

Fig.1: Formation of uric acid from purines

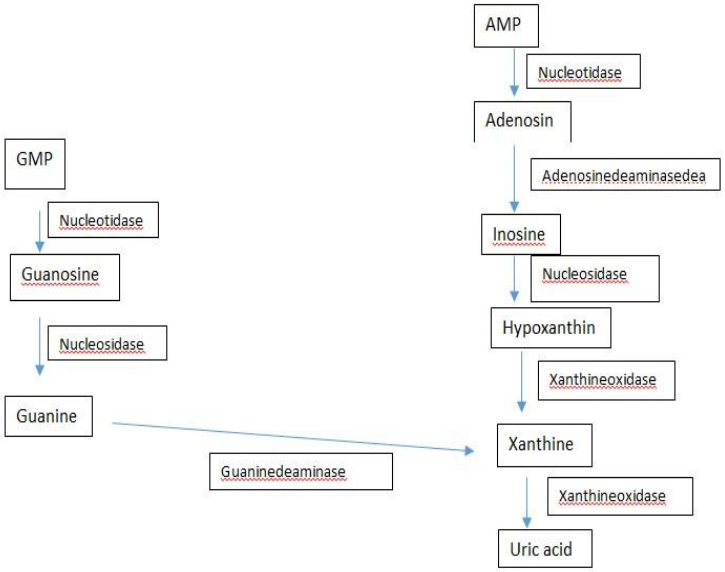

Fig. 2: Enzymatic Degradation of Purine in Humans

As a result, fructose 1-phosphate increases, and intracellular inorganic phosphate concentrations decline. Due to the low supply of phosphate, ATP generation (ADP + Pi) gets limited, and ADP or AMP is catabolized, resulting to Hyperuricemia. There are some other methods to enhance urate concentrations as to intake of sucrose, sorbitol, lactate and methyl xanthines. Sorbitol is absorbed by the body and converted by the liver into fructose, which can lead to an increase in uric acid production [8].Hyperuricemia is a (moderate) risk factor for mortality in medical care because it is considered being a warning sign of cardiovascular disease, diabetes mellitus, renal problems, and inflammation. According to

epidemiological research, UA levels are strongly associated with CVS diseases, including atrial fibrillation (AF), atherosclerosis, hypertension, and heart failure (HF). By monitoring cellular signals including oxidative stress, the inflammatory response, insulin resistance/diabetes, endoplasmic reticulum stress, and endothelial dysfunction Hyperuricemia stimulates the development of cardiovascular diseases [9].

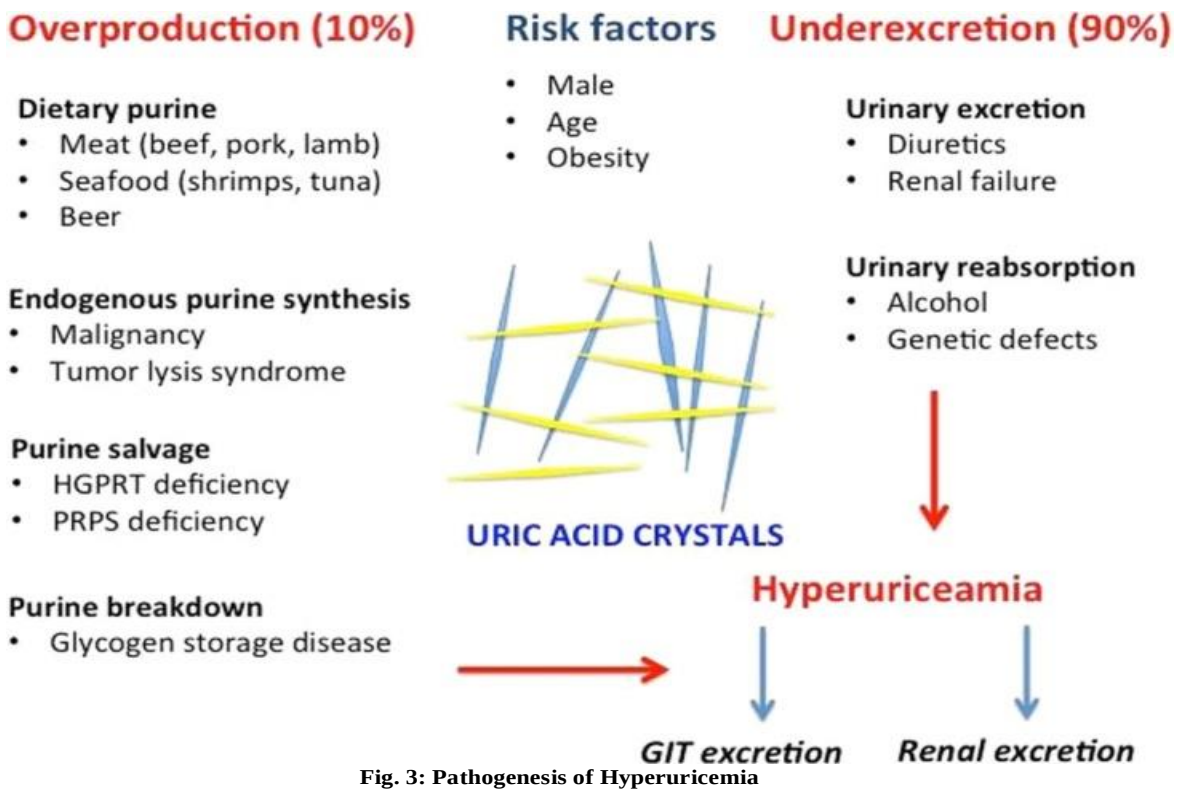

Fig. 3: Pathogenesis of Hyperuricemia

Cardiovascular diseases (CVD) are the first leading cause of death worldwide. This might be due to an increased incidence of chronic illnesses such as obesity, diabetes, hypertension, dyslipidemia, and Hyperuricemia [10].Research has indicated that increased level of uric acid level causes endothelial dysfunction by raising inflammation and oxidative stress. Lesch-Nyhan syndrome is the result of the buildup of high levels of uric acid in the body beginning in infancy, which leads to severe gout, kidney dysfunction, mental retardation, neurological dysfunction, and self-mutilating behaviors. High levels of blood uric acid have long been associated with gout. Gouty arthritis (gout) is a medical condition characterized by red, tender, hot, and swollen joints caused by recurrent attacks of acute inflammatory arthritis. Uric acid levelcan be analyzed in plasma, serum, urine and in exhaled breath condensate. Various methods including phosphortungistic acid methods (PTA), uricase methods, high-performance liquid chromatography methods, dry chemistry systems and biosensor methods employed for the analysis of uric acid concentration. Physiologically, uric acid levels in plasma rise with age; they are lower in women of childbearing age and rise to levels similar to those in men after menopause. Pathological Hyperuricemia caused by a purine/fructose-rich diet, genetic or environmental factors, as well as overproduction from hepatic metabolism and cell turnover, and adrenal under excretion or extra-renal under excretion leads to crystal precipitation in the joints, soft tissue, kidneys, and other organ. It has been well known that uric acid plays significant roles in gout and kidney stones formation. In normal condition, uric acid is excreted through urine. In case of Hyperuricemia, uric acid excretion may be reduced by kidney disease. Additionally, Hyperuricemia occurs when new born babies born with fewer nephrons. In this case a smaller amount of uric acid processed compared to healthy controls, and/or have excessive uric acid transferred from their mothers. chemotherapeutic treatments, leukemia or lymphoma, induce a significant increase in the excretion of uric acid resulting from the nucleic acid metabolism and blockage of renal tubules, causing acute renal failure (tumor lysis syndrome)[11].High uric acid levels can also result from diets rich with purine or fructose or both. Fructose is a specific sugar molecule in that it quickly reduces ATP and increases the uric acid level. However, high diet of purine would be responsible for an increasing only in 1 to 2 mg/dl of Uric acid. It is suggested that people with Hyperuricemia should not take a higher amount of purine-rich food (for instance, bacon, mutton, veal, turkey, pork, kid meat, duck, goose, etc.). Other dietary factors, such as consumption of seafood, meat, sugar-sweetened beverages, and foods high in fructose increased the risk of incident gout, while consumption of dairy products, folate, and coffee was each associated with a lower risk of incident gout and, in some cases, a lower rate of gout flares. Furthermore, foods rich in vitamin C, low fat dairy products, and plant oils such as olive, sun-flower and soy were associated with reduce risk for Hyperuricemia and gout. VitaminC was found to increase renal excretion of uric acid so it can be used as a supplement during management of gout [12].

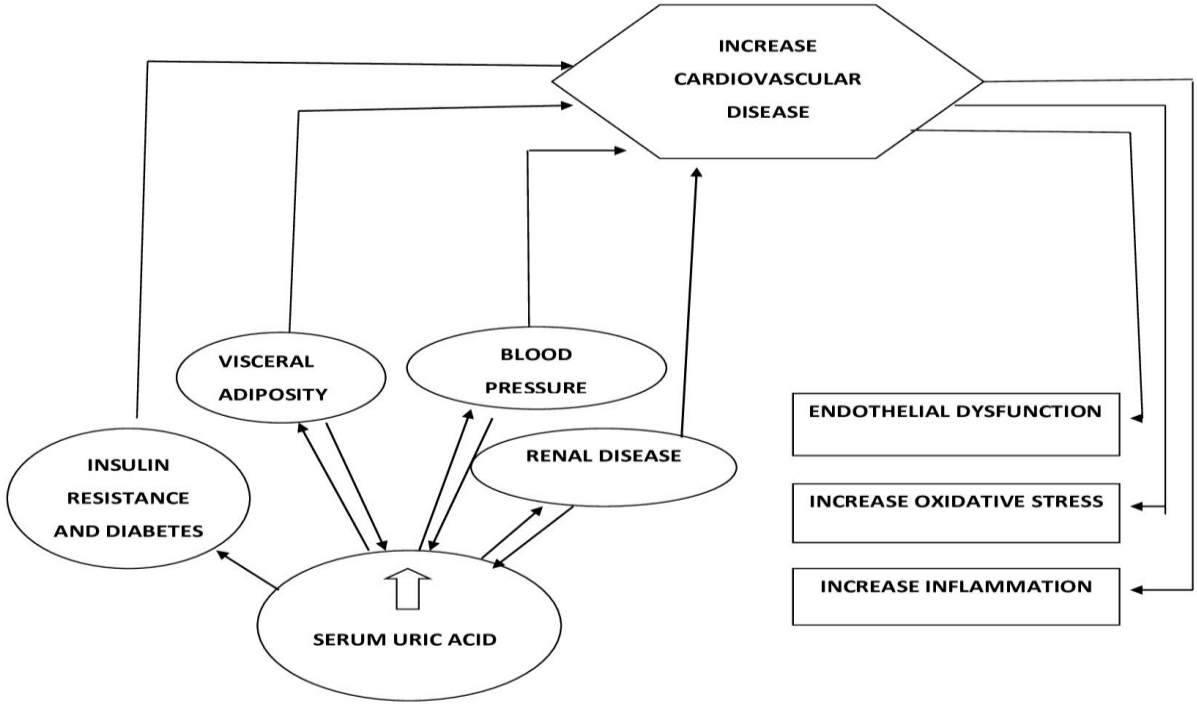

Fig. 4 :Uric acid and related metabolic disorders

Plants are the most abundant suppliers of safe and successful remedies from time immemorial to present either to humans or to other animals. In the treatment of a wide range of acute and chronic illnesses, from the simple cold to sophisticated malignant phases, it is believed that more than 90% of traditional medicine recipes use medicinal herbs including diabetes mellitus, cancer, heart diseases, tuberculosis, asthma, pharyngitis, wound healing, hypertension etc throughout the world[13]. Plants contain various bioactive phytoconstituents such as tannins, flavonoids, alkaloids and polyphenols which have been utilized for treatment of several illnesses because of their various pharmacological properties. More than100 genera of plants which are being used in the indigenous medicinal practices in different part of the world belong to India. India provides the best quality and quantity of medicinal plants and stands second in ranking in terms of export. It is considered as one of the 12 mega biodiversity hot spots of the world with 16 agro-climatic zones and has wide range of about 45,000 plants out of which 7000 plant species are recognized as medicinal plants[14].There are some plants (Table:1) which have various therapeutic values are discussed below:

Table 1: List of Plants having several therapeutic values

S.No.	Synonym	Scientific Name	Family	Traditional Uses
1.	Sweet flag	*Acoruscalamus*	Araceae	Used as gastrointestinal disorders, bronchitis, inflammation, hemorrhoids, cramps and diarrhea. Also used in nerve disorders, appetite loss, bronchitis, chest pain, colic, cramps, diarrhea and rheumatism.[15-16]
2.	Red sandalwood	*Adenanthera pavonina*	Leguminosae	Used in the treatment of diarrhoea, asthma, gout, inflammations, rheumatism, tumor and ulcers[17-18]
3.	Siamese ginger	*Alipinia galanga*	Zingiberaceae	Treat fever, muscle spasm, intestinal gas, rheumatic pain, diabetes and disease of kidney [19-20].
4.	Soursop	*Annona muricata*	Annonaceae	Used for treatment of rheumatism, arthritis, diarrhea and reduce the intestinal acidity [21-22]
5.	Bullock heart	*Annona reticulata*	Annonaceae	Possess properties as analgesic, anti- inflammatory, wound healing, dysentery, cardiac problem, hemorrhage, bacterial infection, fever and ulcer [23-24].
6.	Mug wart	*Artemisia vulgaris*	Asteraceae	Used as tonic to boost energy, stimulate gastric juice and bile secretion, rheumatic swelling of joints [25-26].
7.	Sambong	*Blumea basalmifera*	Asteraceae	Used to cure wounds and cuts, anti-diarrhea, rheumatism, anti-spasms, cold and cough [27-28].
8.	Power puff tree	*Barringtonia racemes*	Lecynthidaceae	Used in treatment of ulcer cancer, pain, inflammation and rheumatic conditions [29-30].
9.	Chinese cassia	*Cinnanmomum cassia*	Lauraceae	Used in Nephropathy, dysmenorrheal, menoxenia arthritis and diabetes and inflammation [31-32].
10.	Indian coral tree	*Erythrina indica*	Fabaceae	Nervine sedative, antiasthmatic, antiseptic, astringent. Inflammatory diseases, urinary tract infections, wounds, diabetes mellitus, and skin and soft tissue injuries [33-34].

11.	Liquorice	*Glycyrrhiza glabra*	Fabaceae	Treat constipation, cough, antimalarial, antioxidant, antispasmodic, antibacterial, peptic ulcer,anti-inflammatory and anti-hyperglycemic properties,hypolipidemic [35-36].
12.	Rosemary	*Rosmarinus officinalis*	Laminaceae	Prevent and cure colds, rheumatism, pain of muscles and joints [37,38].
13.	Devils claw	*Harpagophytum procumbent*	Pedaliaceae	Hardening of arteries, arthritis gout, and muscle pain [39-40].
14.	Bay leaves	*Syzygium polyanthum*	Myrtaceae	Treat diarrhea, rheumatism, and diabetes [41-42].
15.	Celery	*Apium graveolens*	Apiaceae	Anthelmintic, antispasmodic, carminative, diuretic, sedative stimulants, anti-inflammatory effect [43-44].
16.	White willow	*Salix alba*	Salicaceae	Treat painful musculoskeletal joint pain conditions, inflammation, and fever[45-46]
17.	Avocado	*Presea americana*	Lauraceae	Used in diarrhea, dysentery, toothache, skin rashes, infectious processes caused by fungi and bacteria, high blood pressure, diabetes, asthma, intestinal worms, and rheumatism, typhoid fever, malaria, to lower high blood cholesterol, to stimulate uterine contractions and to ease painful menstruations[47-49]
18.	Lily of the valley	*Colchicum autumnale*	Colchicaceae	Used medicinally as a gout suppressant, in the treatment of fever, in veterinary science as an antineoplastic, and in Cardio tonic [50-51].
19.	Bitter gourd	*Momordica charantia*	Cucurbitaceae	Treatment of anemia, bronchitis, Cholera, gout, dysentery, diarrhea gonorrhea rheumatism, ulcer, colic, worms, disease of liver and spleen, cancer and diabetes, lowers cholesterol [52-53].
20.	Satavari	*Asparagus racemosus*	Asparagaceae	Used in female tonic and widely used in diseases including in diabetic retinopathy, tumor, dysentery, bronchitis, inflammations, nervous disorder, hyperacidity, certain infectious diseases, neuropathy, conjunctivitis, spasm, chronic fevers, and rheumatism[54-55].

Conclusion

Uric acid is a catabolic insoluble product of purine metabolism. Uric acid cannot be further broken down by humans. Increased level of uric acid is risk factor for many diseases because it is considered being a warning sign of cardiovascular disease, diabetes mellitus, renal problems, and inflammation. According to epidemiological research, Uric acid levels are strongly associated with CVS diseases including atrial fibrillation (AF), atherosclerosis, hypertension, and heart failure (HF).Plants contain various bioactive phytoconstituents such as tannins, flavonoids, alkaloids and polyphenols which have been traditional utilized for treatment of several illnesses because of their various pharmacological properties. This article analyses the potential impacts of herbal medicines and their therapeutic potential to lower the raised uric acid levels and its related health consequences.

References

1. Jessica Maiuolo, Francesca Oppedisano Santo Gratteri, Carolina Muscoli, Vincenzo Mollace, Regulation of uric acid metabolism and excretion, International Journal of Cardiology 2016;213: 8–14.
2. Ridi El, Rashika Tallima, Hatem, Physiological functions and pathogenic potential of uric acid: A review, Journal of Advanced Research 2017;8(5):487–493.
3. Rehab M. Hafez, Tahany M. Abdel-Rahman, Rasha M. Naguib, Uricacidinplants microorganisms: Biological applications and genetics-A review, Journal of Advanced Research 2017;8:475–486.
4. Singh JA, Reddy SG, Kundukulam J. Risk factors for gout and prevention: a systematic review of the literature. Curr Opin Rheumatol.2011;23 (2):192-202.
5. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA. Uric Acid and Oxidative Stress-Relationship with Cardiovascular, Metabolic, and Renal Impairment. Int J Mol Sci. 2022;16; 23(6):3188.
6. Yuichi Saito and Atsushi Tanaka and Koichi Node and Yoshio Kobayashi, Uric acid and cardiovascular disease: A clinical review, Journal of Cardiology 2021;78(1):51–57.
7. Yu W, Cheng JD. Uric Acid and Cardiovascular Disease: An Update From Molecular Mechanism to Clinical Perspective. Front Pharmacol. 2020; 11:582680.
8. Erick Prado de Oliveira and Roberto Carlos Burini, High plasma uric acid concentration: causes and consequences, Diabetology & Metabolic Syndrome 2012;12:4.
9. . Kushiyama A, Nakatsu Y, Matsunaga Y, Yamamotoya T, Mori K, Ueda K, Inoue Y, Sakoda H, Fujishiro M, Ono H, Asano T. Role of Uric Acid Metabolism-Related Inflammation in the Pathogenesis of Metabolic Syndrome Components Such as Atherosclerosis and Nonalcoholic Steatohepatitis. Mediators Inflamm. 2016; 8603164.
10. Rahimi-Sakak, F., Maroofi, M., Rahmani, J., Bellissimo Nick,Hekmatdoost Azita, Serum uric acid and risk of cardiovascular mortality: a systematic review and dose-response meta-analysis of cohort studies of over a million participants. *BMC* Cardiovascular Disord 2019; 19(1), 218.
11. Jin M, Yang F, Yang I, Yin Y, Luo JJ, Wang H, Yang XF. Uric acid, hyperureicemia and vascular diseases. Front Biosci (Landmark Ed) 2012; Jan1, 17(2):656-69.
12. Gaafar Ragab, Mohsen Elshahaly, ThomasBardin, Gout: Anold disease in new perspective–Areview, Journal of Advanced Research 2017;8:495–511.
13. Akhtar MA. Anti-Inflammatory Medicinal Plants of Bangladesh-A Pharmacological Evaluation. Front Pharmacol. 2022; 13:809324.
14. Murugan, Prasathkumar & Salim, Anisha & Chenthamara, Dhrisya & Robert, Becky & Subrmaniam, Sadhasivam., Therapeutic and pharmacological efficacy of selective Indian medicinal plants -A review. Phytomedicine Plus, 2021; 1(2):100029.
15. Sandeep B. Rajput, Madan B. Tonge, S. Mohan Karuppayil, An overview on traditional uses and

pharmacological profile of *Acoruscalamus* Linn. (Sweet flag) and other Acorus species, Phytomedicine 2014;21:268-276.
16. R. Balakumbahan, K. Rajamani and K. Kumanan, Acoruscalamus: An overview Journal of Medicinal Plants Research, 2010;4(25): 2740-2745.
17. Mujahid, Mohd & Ansari, Vaseem & Sirbaiya, Anup & Kumar, Ranjan & Usmani, Afreen. An insight of pharmacognostic and phytopharmacology study of Adenanthera pavonina. Journal of Chemical and Pharmaceutical Research. 2016;586-596.
18. Ara, & Arifuzzaman, & Ghosh, & Hashem, & Ahmad, & Bachar, Sitesh & Nahar, Dr Lutfun & Sarker, Satyajit.Anti-inflammatory activity of Adenanthera pavonina L., Fabaceae, in experimental animals. Brazilian Journal of Pharmacognosy.2010;20:929-932.
19. Chudiwal, A.K. & Jain, D.P. & Somani, Rahul., Alpinia galanga Willd.- An overview on phyto-pharmacological properties. Indian Journal of Natural Products and Resources,2010; 1:143-149.
20. Ramesh K. Verma, Garima Mishra, Pradeep Singh, K. K. Jha, R. L. Khosa, Alpiniagalanga - An Important Medicinal Plant: A review, Der Pharmacia Sinica, 2011;2 (1): 142-154.
21. Moghadamtousi SZ, Fadaeinasab M, Nikzad S, Mohan G, Ali HM, Kadir HA. Annona muricata (Annonaceae): A Review of Its Traditional Uses, Isolated Acetogenins and Biological Activities. Int J Mol Sci. 2015; 16(7):15625-58.
22. Tai S. Kedari and Ayesha A. Khan, Guyabano (Annona Muricata): A review of its Traditional uses Phytochemistry and Pharmacology, American Journal of Research Communication 2014; 2(10):1.
23. Jamkhande PG, Wattamwar AS. Annona reticulata Linn. (Bullock's heart): Plant profile, phytochemistry and pharmacological properties. J Tradit Complement Med. 2015 Jun 10; 5(3):144-52.
24. Shital S. Chavan , Prashant B. Shamkuwar , Manoj G. Damale and Deepak P. Pawar, A comprehensive review on Annona Reticulata, IJPSR ,2014;14(5):45-50.
25. Ekiert H, Pajor J, Klin P, Rzepiela A, Ślesak H, Szopa A. Significance of *Artemisia Vulgaris* L. (Common Mugwort) in the History of Medicine and Its Possible Contemporary Applications Substantiated by Phytochemical and Pharmacological Studies. Molecules. 2020 Sep 25; 25(19):4415.
26. Kļaviņa A, Keidāne D, Šukele R, Bandere D, Kovaļčuka L. Traditional Latvian herbal medicinal plants used to treat parasite infections of small ruminants: A review. Vet World. 2021 Jun;14(6):1548-1558.
27. Pang, Yuxin & Wang, Dan & Fan, Zuowang & Chen, Xiao-Lu & Yu, Fulai & Hu, Xuan & Wang, Kai & Yuan, Lei. (2014). Blumea balsamifera-A Phytochemical and Pharmacological Review. Molecules (Basel, Switzerland). 19. 9453-9477.
28. Silalahi, M.,Utilization and bioactivity of Blumea balsaminifera (L.) DC. GSC Biological and Pharmaceutical Sciences, 2021;16(2): 224–228..
29. Osman, Nurul & Jaafar sidik, Norrizah & Awal, Asmah. Pharmacological activities of Barringtonia racemosa L. (Putat), A tropical medicinal plant species. Journal of Pharmaceutical Sciences and Research. 2015;7:185-188.
30. Mandana Behbahani,Abdul Manaf Ali,Radzali Muse,Noorjahsn Banu Mohd,Anti-oxidant and anti-inflammatory activities of leaves of Barringtonia racemose, journal of Medicinal Plants Research, 2007;095-102.
31. Zhang C, Fan L, Fan S, Wang J, Luo T, Tang Y, Chen Z, Yu L. *Cinnamomum cassia* Presl: A Review of Its Traditional Uses, Phytochemistry, Pharmacology and Toxicology. Molecules. 2019;24(19):3473.
32. Rao PV, Gan SH. Cinnamon: a multifaceted medicinal plant. Evid Based Complement Alternat Med. 2014:642942.
33. B. Sravan Kumar, D. Narender Prasad, S.Sandhya, K.N.V.Rao, David banji, cultivation, phytochemistry, pharmacological actions and therapeutic applications of *Erythrina Indica*. Lam, International Journal of Applied Biology and Pharmaceutical Technology, 2013; 1(3):858-868.
34. SS Sakat and AR Juvekar., Comparative Study of *Erythrina indica* Lam. (Febaceae) Leaves Extracts for Antioxidant Activity, 2010; 2(1): 63–67.
35. PriyaTyagi, Satish Kumar Sharma &Pawan Kumar, Evaluation of antihyperlipidemic activity of ethanolic root extract of *Glycyrrhizaglabra* Linn. Journal of Drug Delivery and Therapeutics, 2018; 8(6): 20-4.
36. Dastagir, Ghulam & Rizvi, Muhammad, Review – *Glycyrrhiza glabra* L. (Liquorice). Pakistan journal of pharmaceutical sciences. 2016;29 (5): 1727-1733.
37. Andrade JM, Faustino C, Garcia C, Ladeiras D, Reis CP, Rijo P. *Rosmarinus officinalis* L.: an update review of its phytochemistry and biological activity. *Future Sci OA*. 2018; 4(4): FSO283.
38. Borges RS, Ortiz BLS, Pereira ACM, Keita H, Carvalho JCT. *Rosmarinus officinalis* essential oil: A review of its phytochemistry, anti-inflammatory activity, and mechanisms of action involved. J Ethnopharmacol. 2019; 229:29-45.
39. Sankar.P.Mitra, Pharmacology and Biochemistry behind the use of natural herbs to control arthritis,Indian journal of natural products and resources, 2017;8(3):204-223.
40. Schaffer, Larissa & Peroza, Luis & Boligon, Aline & Linde Athayde, Margareth & Alves, Sydney Hartz & Fachinetto, Roselei & Wagner, Caroline, Harpagophytum procumbens Prevents Oxidative Stress and Loss of Cell Viability In Vitro. Neurochemical research, 2013; 38(11): 2256–2267.
41. Ismail, Azlini& Wan Ahmad, Wan Amir Nizam, Syzygium polyanthum (Wight) Walp: A Potential Phytomedicine. Pharmacognosy Journal, 2019; 11:429-438.
42. Mahmoud Dogara A. Review of Ethnopharmacology, Morpho-Anatomy, Biological Evaluation and Chemical Composition of *Syzygium polyanthum* (Wight) Walp. Plant Sci. Today 2022;9(1):167–177.
43. Kooti, Wesam. Ali Akbari, Sara. Asadi-Samani, Majid. Ghadery, Hosna. & Ashtary-Larky, Damoo. A review on medicinal plant of Apium graveolens. Advanced Herbal Medicine. 2015;1: 48-59.
44. Al-Snafi, Ali. The Pharmacology of Apium graveolens. - A Review, International Journal for Pharmaceutical Research Scholars, 2014;3(1):671-677.
45. Tawfeek Nora, Mahmoud Mona F., Hamdan Dalia I, Sobeh Mansour, Farrag Nawaal, Wink Michael, El-Shazly Assem M. Phytochemistry, Pharmacology and Medicinal Uses of Plants of the Genus Salix: An Updated Review, *Frontiers in pharmacology*. vol. 12, 2021,10.3389/fphar.2021.593856.
46. Shara M, Stohs SJ. Efficacy and Safety of White Willow Bark (*Salix alba*) Extracts. Phytother, 2015 Aug; 29(8):1112-6.
47. Tcheghebe, Tene, Nyamen, Linda Dyorisse, Tatong, Francis, Seukep, Armel Jackson. Ethnobotanical uses, phytochemical and pharmacological profiles, and toxicity of persea Americana mill.: An overview, 2016/12/30,vol-3:213-221.

48. Pamplora, G.D., Roger, M.D., Encyclopedia of Medicinal Plants. 1999; 719 -720.
49. Afzal, Muhammad. Akhtar, Attiq, Bukhari, Riaz, Ul Hasan, Syed Zia, SYED, Haseeb. A Review on Avocado Fruit: Description, Morphological Characteristics, Composition, Nutritional Benefits and Propagation, Plant Cell Biotechnology and Molecular Biology, 2022:32-41.
50. Akram, Muhammad. Alam, Osama. Usmanghani, Khan. Naveed, Akhtar.Asif, Muhammad. Colchicum autumnale: A review. Journal of Medicinal Plants Research. 2012; 6: 1489-1491.
51. Dalbeth N, Lauterio TJ, Wolfe HR. Mechanism of action of colchicine in the treatment of gout. Clin Ther. 2014 Oct 1;36(10):1465-79.
52. Ahmad N, Hasan N, Ahmad Z, Zishan M, Zohrameena S. Momordica Charantia: For Traditional Uses and Pharmacological actions. JDDT, 14Mar.2016, 6(2):40-4.
53. K.P.Sampath Kumar, Debjit Bhowmik, Traditional Medicinal Uses and Therapeutic Benefits of Momordica Charantia Linn, International Journal of Pharmaceutical Sciences Review and Research, 2010; 4(3):23-28.
54. Hasan, Noorul. Ahmad, Nesar. Zohrameena, Shaikh. Khalid, Maad. Akhtar, Juber. Asparagus Racemosus: for medicinal uses & pharmacological actions, International Journal of Advanced Research. 2016:259-267.
55. Sharma, Arti. Sharma, Vandana,. A Brief review of medicinal properties of *Asparagus racemosus* (Shatawari), International Journal of Pure & Applied Bioscience. 2013; 1(2): 48-52: 2320 – 7051.

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