Potential of medicinal plants in management of diabetes: An updates

Lochana L. Malode 1, Jagdish V. Manwar 1, Wrushali A. Panchale 2,*, Shivam A. Bartere 1, and Ravindra L. Bakal 2

1 IBSS’s Dr. Rajendra Gode College of Pharmacy, Mardi Road, Amravati-444 602, Maharashtra, India.
2 IBSS’s Dr. Rajendra Gode Institute of Pharmacy, Mardi Road, Amravati-444 602, Maharashtra, India.

GSC Advanced Research and Reviews, 2021, 08(01), 149–159

Publication history: Received on 12 June 2021; revised on 22 July 2021; accepted on 24 July 2021

Article DOI: https://doi.org/10.30574/gscarr.2021.8.1.0151

Abstract

Phytochemical means plant derived chemicals they are defined as bioactive nutrient present in plant in fruits, vegetables, grains, and other part of plants that may provide advantageous health benefits across basic nourishment. Medicinal plants are used in the treatment of various illness due to the presence of therapeutically important phytochemicals. Sometimes in patients with diabetes mellitus, the levels of antioxidant parameters are found to decrease, hence in many studies phytochemicals are suggested to improve the insulin sensitivity. Some phytocompounds such as flavonoids, prophenyl phenols, are also found effective in the complications of diabetes. The major challenging issue in diabetes management is the obstruction of various complications that remain the main cause of diabetes-related mortality. This review mainly focuses on the relationship between diabetes mellitus and preventive roles of various phytochemicals on diabetes.

Keywords: Diabetes; Classification; Aloe vera; Allium cepa; Gymnema sylvestre

Graphical Abstract

1. Introduction

Now a days, medicinal plants-based formulation has gained much more attention of various researchers across the world. The popularity of herbal plants or medicines are not only because of easily availability but also worldwide patient compliance and esthetic value. Even today, peoples from tribal areas and villages are mostly depends on the use of...
traditional system of medicine for the treatment of various diseases or disorders. Some of the medicinal plants that are commonly used are Withania somnifera (ashwagandha), Capsicum annuum (capsicum), Hypericum perforatum (St. John's wort), Aloe barbadensis (Aloe vera), Oroxyllum indicum, etc. Other plants or parts their of used as condiments includes Allium sativum (garlic), Allium cepa (onion), Elettaria cardamomum (cardamom), Cuminum cyminum (cumin), Myristica fragrans (nutmeg), Piper nigrum(black pepper), Madhuca indica etc are also being used in the kitchen [1-16].

They not only finds their use in t Phytochemicals from the Greek word Phyto means plant are biologically active, naturally occurring chemical compounds detected in plants, which provide health benefits for humans further than those allotted to macronutrients and micronutrients [17]. They protect plants from illness and damage and provide to the plant’s color, aroma, and flavor. In general, the plant chemicals that keep safe plant cells from environmental hazards such as pollution, stress, pressure, the rush of air UV exposure, and pathogenic attacks are called phytochemicals [18].

In broad-ranging dietary phytochemicals are found in fruits, vegetables, legumes, whole grains, nuts, seeds, fungi, herbs, and spices [19]. Recently, it is known that they have a part in the protection of human health when their dietary intake is significant. Broccoli, cabbage, carrots, onions, garlic, entire wheat bread, tomatoes, grapes, cherries, strawberries, raspberries, beans, legumes, and foods are common sources. Phytochemicals gather in different parts of the plants, such as in the roots, stems, leaves, flowers, fruits, or seeds [20]. World Health Organization (WHO) says that world’s 80% population, presently uses medicines of plant origin for their prime health care [20].

Diabetes could be a illness that happens once your glucose, conjointly referred to as blood glucose, is just too high. Glucose is your main supply of energy and comes from the food you eat. Insulin, an endocrine hormone secreted by the exocrine gland, helps aldohexose from food get into your cells to be used for energy. Generally in diabetes your body doesn’t build enough of any hypoglycemic agent or doesn’t use hypoglycemic agent well, aldohexose then stays in your blood and doesn't reach your cells [22]. Polygenic disease could be a chronic disorder of sugar, fat and super molecule metabolism characterized by enlarged fast [23].

Studies conducted in Asian nation within the last decade have highlighted that the prevalence of polygenic disease is increasing speedily within the urban population. DM maybe one among the oldest diseases far-famed to man [24-26]. The enlarged glucose in DM results in several complications like metabolic changes, enlarged aerophilous stress, vessel and urinary organ diseases [27].

2. Classification of Diabetes

There are many different forms of diabetes mellitus. So far, scientists have been evaluating, and classifying some of these species, and to determine its prevalence in the general population. The most common types of diabetes are type 1, type 2, and gestational diabetes [28]. Type 1 diabetes are due to the auto-immune-cells which are destroyed, it usually leads to absolute insulin deficiency. If you have type 1 diabetes, your body doesn’t produce insulin. Your immune system attacks and destroys cells in the pancreas that produce insulin [29].

Type 1 diabetes is usually diagnosed in children and young adults, but can occur at any age. People with type 1 diabetes must use insulin every day in order to stay alive [30]. Type 2 diabetes are due to the progressive loss of insulin secretion by the cells, which is often, due to insulin resistance. If you have type 2 diabetes, your body doesn’t produce or use insulin well. Type 2 Diabetes can develop at any age, even during childhood. However, this type of diabetes usually occurs in middle-aged and older people.

Type 2 is the most common form of diabetes. Gestational diabetes was diagnosed in the second or third trimester of pregnancy, which is clearly not the overt diabetes prior to pregnancy. Some women develop diabetes during pregnancy. In most of the cases, this type of diabetes can be fixed after the baby is born. However, if you have gestational diabetes, you are more likely to develop type 2 diabetes later in life [30-34].

3. Medicinal Plants

Following medicinal plants have a vast potential in the treatment of various ailments due to the presence of therapeutically important phytochemicals. All the plants listed in this review are native to Asian countries and are routinely used by the traditional practitioners for the treatment of diabetes.
3.1. Syzygium cumini

Syzygium cumini (family myrtaceae) is likewise called syzygium jamunum and Eugenia cumini. Other common place names are jamul, black plum, java plum, Indian blackberry, jamblang, jamun and many others. The jamun has obtained some distance extra popularity in folk medicine and within the pharmaceutical exchange than in every other area [35-36]. Medicinally, the fruit is said to be astringent, stomachic, carminative, antiscorbutic and diuretic moreover, a fruit extract confirmed antimicrobial and cytotoxic activities and may potentially be used on normal antimicrobial merchandise [37]. Some of the patients had shown manipulate of blood sugar ranges when they had been placed on jamun remedy indicating a terrific response to the treatment, whereas others did now not show any development after the treatment [38-39].

3.2. Aloe vera

Aloe Vera may be a common name for Aloe barbadensis, that is that the most widely-used species of aloe. Aloe, a well-liked flora, includes a long history as a utile folks remedy. The plant will be separated into 2 basic products: gel and latex. Aloe vera gel is that the leaf pulp or mucilage, aloe latex, normally spoken as “aloe juice,” may be a bitter yellow exudate from the pericyclic tubules simply to a lower place the outer skin of the leaves [40-44].

3.3. Zingiber officinale

Zingiber officinale, regularly called Ginger, belongs to the family of family Zingiberaceae and is taken into account to be a very important spice with multitudinous health advantages. The rhizomes of ginger are used historically for the treatment of cardiovascular disease, diabetes, arthritis, sprain, muscular aches, sore throats, fever, cramps, gingivitis, toothache, asthma. Ginger shows effective glycaemic management properties in diabetes [45]. The mechanisms underlying these actions area unit related to the inhibition of key enzymes dominant macromolecule metabolism and accumulated internal secretion release/sensitivity, leading to increased aldoxose uptake in peripheral fat and musculus tissues. The outstanding super molecule lowering effects of ginger additionally contribute to up the internal secretion resistant condition. the foremost active ingredients in ginger area unit the pungent principles, gingerols, and shogaol. Ginger has shown outstanding protecting effects on diabetic liver, kidney, eye, and neural system complications [46-49].

3.4. Allium cepa

The species onion L., normally called onion, has been for a protracted time thought-about a member of the family Liliaceae, taxonomic category Allioideae. Allium cepa is additionally antioxidant and hypolipidaemic activity. Administration of a sulfur containing aminoalkanoic acid from onion, S-methyl amino acid sulphoxide (SMCS) to alloxan iatrogenic diabetic rats considerably controlled glucose yet as lipids in blood serum and tissues and normalized the activities of liver hexokinase, aldoxose 6-phosphatase and HMG Co A enzyme [39-41].

Onion is made in many phytonutrients that square measure recognized as necessary components of the Mediterranean diet however it's received attention conjointly for its biological properties and potential application within the treatment and interference of variety of diseases a large style of phytochemicals as well as the flavonoids, alkaloids, sulfides, saponins, polysaccharides, polyphenols, and several other compounds of the sulfur containing amino acids amino acid are known as main constituents of those plants [42-44].

3.5. Allium sativum

The species sativum., usually known as Garlic, belong to the family Amaryllidaceae. The vital herbs that are used from earlier period as ancient drugs. This result is assumed to flow from to redoubled internal organ metabolism, redoubled hormone unleashes from exocrine gland beta cells and/or hormone frugal result. S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, may be a sulfur containing aminoalkanoic acid, that controlled super molecule peroxidation higher than glibenclamide and hormone. SACS additionally stirred in vitro hormone secretion from beta cells isolated from traditional rats with the exception of this, alliaceous plant exhibits antimicrobial, antitumour and cardioprotective activities [45-51].
3.6. *Azadirachta indica*

The species *Azadirachta indica*. regularly called as a Neem belongs to the family Meliaceae. Apart from having anti-diabetic activity, this plant also has anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects. The non-wood products of neem like flowers, leaves, bark, fruits, seeds (oil, cake), and gum also find various uses. The Neem plant shows various biological activities like antibacterial, antifungal, insecticidal and other activities. It causes hypoglycemia and peroxidation of lipid metabolites while increasing the enzymatic activities of glutathione peroxidases, catalases and superoxide dismutases to enhance the antioxidation [52-60].

3.7. *Coriandrum sativum*

*Coriandrum sativum* L., a member of the Apiaceae family, is a commonly used food ingredient possessing medicinal as well as nutritional properties. Administration of ethanolic stem and leaves extract of coriander to alloxan-induced diabetic. Sub-chronic administration of aqueous extract of coriander seeds to hyper-caloric diet fed Merionesshawir rats resulted in normalization of blood glucose levels with improved insulin resistance and decreased levels of total cholesterol and triglycerides [60-61].

3.8. *Gymnema sylvestre*

Gymnema derives from the Greek words gymnos and name meaning "naked" and "thread", respectively. The Hindi and Urdu name gurmar, mean "sugar destroyer". The leaves and extracts contain gymnemic acids, the major bioactive constituents that interact with taste receptors on the tongue to temporarily suppress the taste of sweetness [62-65].
3.9. Acacia arabica (Babul)

The antidiabetic effects of hydroalcoholic extracts of Acacia Arabica investigated in diabetic rats. The Alloxan monohydrate was used to induce the diabetes in normal rats. The plant extract acts as an antidiabetic agent by acting as secret gouge to release insulin. A. arabica when administered (2, 3 and 4 g/kg body weight) to normal rabbits, induces hypoglycemic effect by initiating release of insulin from pancreatic beta cells [66]. For all plants, see Fig. 1 and for important phytoconstituents refer Table 1.

**Table 1. Active Phyoconstituents and their structure with pharmacological activity**

| Plant                  | Active constituent       | Pharmacological activity                                                                 |
|------------------------|--------------------------|------------------------------------------------------------------------------------------|
| Syzygium cumini        | (-)-Epicatechin (Flavonoid) | Hypoglycemic, anti-oxidant activity, Anti-hyperglycemic effect                           |
|                        | Marsupsin                | Hypoglycemic, anti-oxidant activity, Anti-hyperglycemic effect                           |
| Aloe vera (L.)         | Lophenol (Phytosterols)  | Anti-hyperglycemic activity with protective effect on pancreas, liver and small intestine. |
| Zingiber officinale    | Gingerol                 | Anti-inflammatory, antidiabetic, antidyslipidemia, hypotensive, vasodilator, antiobesity, anticancer agent |
|                        | Shogaoi                  | Anti-inflammatory, antidiabetic, antidyslipidemia, hypotensive, vasodilator, antiobesity, anticancer agent |
| Allium cepa            | SMCS                     | S-Methyl cysteine sulfoxide (SMCS) showed antidiabetic, Hyperlipidemic activity.           |
| Allium sativum         | Allicin                  | S-allyl cysteine (SACS) showed beneficial effect on antioxidant system; SACS showed anti-diabetic activity. |
|                        | Diallylthiosulfinate      | Allicin lowered the blood pressure and improved lipid profile in hyperlipidemic, hyperinsulinemic Anti-diabetic activity. |
| Azadirachta indica     | β-Sitosterol (steroid)   | Hypoglycemic activity, Hypoglycemic and restricted oxidative stress, Anti-hyperglycemic activity. |
|                        | Gymnemic acids IV (R1 = tigloyl, R2= H, R3 = glucuropyranosyl) | Reduced intestinal glucosidase activity, ant hyper glycemic properties, Anti-diabetic activity |
| Coriandrum sativum L   | Maltase (α- glucosidase)   | Anti-hyperglycemic, Anti-diabetic activity                                                |
| Gymnema masyvestre     | Gymnemic acid Saponin     | Anti-hyperglycemic effect, Anti-diabetic activity,                                          |
| Acacia arabica         | Tannin, Flavonoids       | anti-microbial, anti-plasmodial, antioxidant activity, Anti-diabetic activity.             |

4. **Analysis of phytochemicals**

There are many analytical tools that can be used for the analysis of various phytochemicals in different plants. These methods include UV-spectrophotometry, gas chromatography, HPLC, HPTLC, etc [67-111].
5. Conclusion

As whole world is facing a problem of diabetes, use of plant based medicines has established itself as a ray of hope for in treatment of it with patient safety and better acceptance. Using the herbal medicines, we can keep the control on blood sugar level. It is quite evident from this review that the phytochemicals discussed are important in management of all types of types of diabetes. In addition, there is urgent need to explore such types of more plants that could show anti-diabetic activity.

Acknowledgments

We express our sincere thanks to Shri. Yogendraji Gode and Dr. Yogeshji Gode, IBSS's Dr. Rajendra Gode College of Pharmacy, Amravati and Dr. Rajendra Gode Institute of Pharmacy, Amravati.

Disclosure of conflict of interest

The author declares no conflict of interest.

References

[1] Badukale NA, et al. Phytochemistry, pharmacology and botanical aspects of Madhuca indica: A review. Journal of Pharmacognosy and Phytochemistry. 2021; 10(2): 1280-1286.
[2] Khadatkar SN, et al. Preparations and evaluation of microcapsules of capsaicin. International Journal of Chemical Sciences. 2007; 5(5): 2333-2341.
[3] Sahare AY, et al. Hypericum perforatum: A Medicinal plant. Plant Archives. 2007; 7(2): 463-468.
[4] Manmode R, et al. Effect of preparation method on antioxidant activity of ayurvedic formulation kumaryasava. J Homeop Ayurv Med. 2012; 1: 114.
[5] Padgilwar S, et al. Traditional uses, phytochemistry and pharmacology of Oroxylum Indicum: A Review. International Journal of Pharmaceutical and Phytopharmacological Research. 2014; 3(6): 483-486.
[6] Manwar J, et al. Isolation, biochemical and genetic characterizations of alcohol-producing yeasts from the flowers of Woodfordia fruticosa. J Young Pharm. 2013; 5(4): 191-194.
[7] Wadekar AB, et al. Morphology, phytochemistry and pharmacological aspects of Carica papaya, an review. GSC Biological and Pharmaceutical Sciences. 2020; 14(03): 234-248.
[8] Khadatkar SN, et al. In-vitro anthelmintic activity of root of Clitoria ternatea linn. 2008; 4(13): 148-150.
[9] Sahare AY, et al. Antimicrobial activity of Pseudarthria viscida roots. Asian Journal of Microbiology Biotechnology & Environmental Sciences. 2008; 10(1): 135-136.
[10] Gudalwar BR, et al. Allium sativum, a potential phytopharmacological source of natural medicine for better health. GSC Advanced Research and Reviews. 2021; 06(03): 220–232.
[11] Malode GP, et al. Phytochemistry, pharmacology and botanical aspects of Murraya Koenigii in the search for molecules with bioactive potential - A review. GSC Advanced Research and Reviews. 2021; 06(03): 143–155.
[12] Manmode R, et al. Effect of preparation method on antioxidant activity of ayurvedic formulation kumaryasava. J Homeop Ayurv Med. 2012; 1: 114.
[13] Padgilwar S, et al. Traditional uses, phytochemistry and pharmacology of Oroxylum Indicum: A Review. International Journal of Pharmaceutical and Phytopharmacological Research. 2014; 3(6): 483-486.
[14] Nikhare AM, et al. Morphological, Phytochemical and pharmacological aspects of Syzgium Cumini. International Journal of Medical, Pharmaceutical and Biological Sciences. 2021; 1(1): 1-11.
[15] Parbat AY, et al. Ethnopharmacological review of traditional medicinal plants as immunomodulator. World Journal of Biology Pharmacy and Health Sciences. 2021; 06(02): 043–055.
[16] Dongare PN, et al. An Overview on herbal cosmetics and cosmeceuticals. Int J Pharm Sci Rev Res. 2021; 68(1): 75-78.
Hasler CM, Blumberg JB. Phytochemicals: biochemistry and physiology. Introduction. J Nutr. 1999; 129(3): 756S-757S.

Gibson EL, Wardle J, Watts CJ. Fruit and vegetable consumption, nutritional knowledge and beliefs in mothers and children. Appetite. 1998; 31(2): 205-28.

Mahan LK, Escott-Stump S. Krause’s Food, Nutrition & Diet Therapy. 10th Edition, W.B. Saunders Co., Pennsylvania. 2000.

Saxena M, Mir AH, Sharma M, Malla MY, Qureshi S, Mir MI, Chaturvedi Y. Phytochemical screening and in-vitro antioxidant activity isolated bioactive compounds from Tridax procumbens Linn. Pak J Biol Sci. 2013; 16(24): 1971-7.

Kooti W, Farokhipour M, Asadzadeh Z, Ashtary-Larky D, Asadi-Samani M. The role of medicinal plants in the treatment of diabetes: a systematic review. Electron Physician. 2016; 8(1): 1832-1842.

Kaul K, Tarr JM, Ahmad SI, Kohner EM, Chibber R. Introduction to diabetes mellitus. Adv Exp Med Biol. 2012; 771: 1-11.

Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. J Clin Biochem Nutr. 2007; 40(3): 163-73.

Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J. 2014; 7(1): 45-48.

Ahmed AM. History of diabetes mellitus. Saudi Med J. 2002; 23(4): 373-8.

Mukhtar Ya’U, Yunusa Umar, AM, Galalain. A Modern Overview on Diabetes Mellitus: A Chronic Endocrine Disorder. 2019.

Kharrroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. World J Diabetes. 2015; 6(6): 850-867.

American Diabetes Association. Standards of medical care in diabetes--2011. Diabetes Care. 2011; 34 Suppl 1(Suppl 1): S11-S61.

Latha S, kumar R. The Facts about Diabetes Mellitus- A Review .Galore International Journal of Health Sciences and Research. 2019; 4: 2456-9321.

Alamgir ANM. Biotechnology, In Vitro Production of Natural Bioactive Compounds, Herbal Preparation, and Disease Management (Treatment and Prevention). Therapeutic Use of Medicinal Plants and their Extracts: Volume 2. 2018; 74: 585-664.

Bacanli M, Dilsiz SA, Başaran N, Başaran AA. Effects of phytochemicals against diabetes. Adv Food Nutr Res. 2019;89:209-238.

Sridharan K, Mohan R, Ramaratnam S, Panneerselvam D. Ayurvedic treatments for diabetes mellitus. Cochrane Database Syst Rev. 2011;(12):CD008288.

Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J. 2012;27(4):269-273.

Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care. 2008 May; 31(5): 899-904.

Hameed A, Dirar M, Doupias J. Gestational diabetes from A to Z. World J Diabetes. 2017; 8(12): 489-506.

GaikwadSB, Mohan GK, Rani MS. Phytochemicals for Diabetes Management .Pharmaceutical Crops.2014; 5(1): 11-28.

Marín-Peñalver JJ, Martín-Timón I, Sevillano-Collantes C, Del Cañizo-Gómez FJ. Update on the treatment of type 2 diabetes mellitus. World J Diabetes. 2016;7(17):354-395.

Muniappan A, Pandurangan SB.Syzygium cumini (L.) Skeels: A review of its phytochemical constituents and traditional uses.American Pacific Journal of Tropical Biomedicine.2012; 2(3):240-6.

Jagetia GC. A review on the role of jamun, syzygium cumini skeels in the treatment of diabetes. International Journal of Complementary & Alternative Medicine.2018; 11(2):91-95.

Ramteke V, Kurrey V, Kar S Jamun. A Traditional Fruit and Medicine. Popular Kheti. 2015; 3(3): 188-190.
[41] Helmstäder A. Syzygiumcumini(L.) (Myrtaceae) against diabetes –125 years of research. Pharmazie. 2008;63(2):91–10.

[42] SharmaVI, SoniMK, Onkar JM, Sharma O. Medicinal uses of jamun [Syzygiumcumini (Linn) Skeel.]: A Review. Article World Journal of Pharmaceutical and Medical Research. 2019;5(8): 89-90.

[43] Moghaddasi MS, Verma SK. Aloe vera their chemicals composition and applications: A review. International Journal of Biological & Medical Research. 2011; 2(1): 466-471.

[44] Spoorthy NB, Noor A. Bioactive constituents of the genus Aloe and their potential therapeutic and pharmacological applications: A review. Journal of Applied Pharmaceutical Science. 2020;10(11): 133-145.

[45] Alethia Muñiz-Ramirez, Rosa M Perez, Efren Garcia, Fabiola E. Garcia. Antidiabetic Activity of Aloe vera Leaves. Evidence-Based Complementary and Alternative Medicine. 2020;6371201:9.

[46] Marta Sánchez, Elena González-Burgos, Irene Iglesias, M Pilar Gómez-Serranillos. Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. Molecules. 2020;25(6): 1324.

[47] Josias H. Hamman Composition and Applications of Aloe vera Leaf Ge Molecules. 2008; 13(8): 1599–1616.

[48] MarzannaHęś, Krzysztof Dziedzic, Danuta Górecka, Anna Jedrusek-Golińska, ElżbietaGujska Aloe vera (L.) Webb. Natural Sources of Antioxidants – A Review. Plant Foods for Human Nutrition. 2019;74:255–265.

[49] AmeurBenYounes, Maryem Ben Salem, Hanen ElAbed, Raoudhajarraya Phytochemical Screening and Antidiabetic, Anti-hyperlipidemic, and Antioxidant Properties of Anthyllis henoniana (Coss.) Flowers Extracts in an Alloxan-Induced Rats Model of Diabetes. Evidence-Based Complementary and Alternative Medicine, Article. 2018; 8516302: 14.

[50] Yiyi Zhang, Wen Liu, Dan Liu, Tiejun Zhao, Haoming Tian. Efficacy of Aloe Vera Supplementation on Prediabetes and Early Non-Treated Diabetic Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Nutrients 2016; 8:388.

[51] Hanadika R, SaldanaEA, Sunita V, Palatty PL, Fayad R, BaligaMS. A review of the gastroprotective effects of ginger (Zingiber officinale Roscoe). Food Funct 2013; 4(6):845–855.

[52] Gloria Aderonke Otunola, Anthony Jide Afolayan. A Review of the Anti-diabetic Activities of Ginger A Review of the Antidiabetic Activities of Ginger.

[53] Wu KL, Rayner CK, Chuah SK. Effects of ginger on gastric emptying and motility in healthy humans. European Journal of Gastroenterology & Hepatology. 2008;20(5):436-440.

[54] Nammi S, Satyanarayana S, Basil DR. Protective effects of ethanolic extract of Zingiber officinale rhizome on the development of metabolic syndrome in high-fat diet-fed rats. Basic & Clinical Pharmacology & Toxicology. 2009;104(5):366–373.

[55] Mariangela M, Valentina A, Giancarlo S, Filomena C. Biological Properties and Bioactive Components of Allium cepa L.: Focus on Potential Benefits in the Treatment of Obesity and Related Comorbidities. Molecules. 2019;24(1):119.

[56] Najeebullah S, Khan SZ, Ahmad JS, Khan I, Ali M. Ethno-Medicinal and Phytochemical Properties Of Genus Allium: A Review Of Recent Advances. Pak. J. Bot. 2021; 53(1): 135-144.

[57] Roman-Ramos R, Flores-Saenz JL, Alaricon-Aguilar FJ. Antihyperglycemic effect of some edible plants. J. Ethnopharmacol. 1995; 48: 25–32.

[58] Kumari K, Mathew BC, Augusti KT. Antidiabetic and hypolipidaemic effects of S-methyl cysteine sulfoxide, isolated from Allium cepa Linn. Ind. J. Biochem. Biophys. 1995;32:49–54.

[59] Mathew PT, Augusti KT. Hypoglycemic effects of onion, Allium cepa Linn. on diabetes mellitus- a preliminary report. Ind. J. Physiol. Pharmacol. 1975;19: 213–217.

[60] Böttcher C, Krähmer A, Stürtz M, Widder S, Schulz H. Effect of cultivar and cultivation year on the metabolite profile of onion bulbs (Allium cepa L.). J. Agric. Food Chem. 2018;66: 3229–3238.

[61] Lim TK. Modified Stems, Roots, Bulbs. In Edible Medicinal and Non-Medicinal Plants; Springer: Dordrecht, The Netherlands. 2015; 9:124–203.

[62] Ayaz E, Alposy HC. Garlic (Allium sativum) and traditional medicine. TurkiyeParazitolojiiDerg. 2007;31:145–149.
[84] Sahare AY, et al. Antimicrobial activity of Pseudarthria viscida roots. Asian Journal of Microbiology Biotechnology & Environmental Sciences. 2008; 10(1):135-136.

[85] Manwar JV, et al. Experimental design approach for chromatographic determination of ketorolac tromethamine from bulk drug and tablet formulation. Global Journal of Pharmacy & Pharmaceutical Sciences. 2017;3(2):38-47.

[86] Shubham Garibe, et al. Bioequivalence study of test formulations T1 and T2 Nadolol tablets USP with reference formulation in healthy adult, human subjects under fed conditions. Ijppr.Human. 2021; 20(2):20-28.

[87] Chaudhari KD, et al. Comprehensive review on characterizations and application of gastro-retentive floating drug delivery system. GSC Advanced Research and Reviews. 2021; 07(01):035-044.

[88] Chaudhari KD, et al. Floating drug delivery system: An update of preparation and classification of formulation. Ijppr.Human. 2021; 21(1):207-220.

[89] Manmode RS, et al. Stability indicating HPLC method for simultaneous determination of methocarbamol and nimesulide from tablet matrix. Der Chemica Sinica.2011;2(4):81-85.

[90] Malode GP, et al. Preparation and evaluation of a novel floating in situ gel system for the treatment of peptic ulcer. World Journal of Pharmacy and Pharmaceutical Sciences. 2021; 10(2):47-54.

[91] Jain CM, et al. Review on approaches for development and evaluation of extended-release tablets. Review on approaches for development and evaluation of extended-release tablets. World Journal of Pharmacy and Pharmaceutical Sciences. 2021;10(4):542-554.

[92] Nimbalwar MG, et al. A brief review on principle, preparation and properties of proniosomes: A vesicular drug delivery system. World J Pharm Sci. 2021; 9(5): 149-162.

[93] Bagade SB, et al. Simultaneous high performance thin layer chromatographic estimation of methocarbamol and nimesulide in combined dose tablet. Journal of Pharmaceutical Research. 2006;5(4):137-140.

[94] Vaidya VM, et al. Design and in vitro evaluation of mucoadhesive buccal tablets of terbutaline sulphate. Int J PharmTech Res. 2009; 1(3): 588-597.

[95] Dhamankar AK, et al. The novel formulation design of O/o ketoprofen for improving transdermal absorption. Int J of Pharm Res. 2009; 4(1 Suppl): 1449-1457.

[96] Manwar JV, et al. Didclofenac Sodium Loaded Nanosized Ethosomes: An Investigation on Z-Average, Polydispersity and Stability. J Pharm Res. 2017; 1(3): 000115.

[97] Patil SS, et al. Ultrasound-Assisted Facile Synthesis of Nanostructured Hybrid Vesicle for the Nasal Delivery of Indomethacin: Response Surface Optimization, Microstructure, and Stability. AAPS PharmSciTech. 2019;20(3):97.

[98] Nimbalwar MG, et al. Fabrication and evaluation of ritonavir proniosomal transdermal gel as a vesicular drug delivery system. Pharmacophore. 2016; 7(2): 82-95.

[99] Pophalkar PB, et al. Development and evaluation of ondansetron medicated jelly. World Journal of Pharmaceutical Research. 2018; 7(19): 1252-1263.

[100] Suroshe RS, et al. Development and characterization of osmotic drug delivery system of model drug. World Journal of Pharmaceutical Research. 2018; 7(18): 1158-1171.

[101] Kadam CY, et al. Design and In vitro characterization ofophase transition system using grivastigmine tartrate for nasal drug delivery system. World Journal of Pharmaceutical Research. 2018; 8(1): 815-829.

[102] Gulhane CA, et al. UV-Visible Spectrophotometric estimation of azithromycin and cefixime from tablet formulation by area under curve method. World Journal of Pharmaceutical Sciences.2021; 9(6): 163-168.

[103] Motule AS, et al. Development and physicochemical evaluation of bilayered transdermal patches of ondansetron hydrochloride Journal of Innovations in Pharmaceutical and Biological Sciences. 2021; 8(3): 17-23.

[104] Vohra M, et al. Bioethanol production: Feedstock and current technologies. Journal of Environmental Chemical Engineering. 2014; 2 (1):573-584

[105] Manwar J, et al. Comparative antioxidant potential of Withania somnifera based herbal formulation prepared by traditional and non-traditional fermentation processes. Integrative Medicine Research.2013; 2: 56–61.
[106] Manwar JV, Mahadik KR, Paradkar AR, Takle SP, Sathiyanarayanan L, Patil SV. Determination of withanolides from the roots and herbal formulation of Withania somnifera by HPLC using DAD and ELSD detector. Der Pharmacia Sinica. 2012; 3: 41–46.

[107] Manwar J, Mahadik K, Paradkar A. Plackett-Burman design: A statistical method for the optimization of fermentation process for the yeast Saccharomyces cerevisiae isolated from the flowers of Woodfordia fruticosa. Fermentation Technology. 2013; 2: 109. http://dx.doi.org/10.4172/2167-7972.1000109.

[108] Manwar J, Kumbhar DD, Bakal RL, Baviskar SR, Manmode RS. Response surface based co-optimization of release kinetics and mucoadhesive strength for an oral mucoadhesive tablet of cefixime trihydrate. Bulletin of Faculty of Pharmacy. Cairo University. 2016; 54: 227–235. http://dx.doi.org/10.1016/j.bfopcu.2016.06.004

[109] Manwar JV, Sonawane BV, Patil SV, Takle SP. Rapid RP-HPLC method for estimation of zidovudine from tablet dosage form. Der Chemica Sinica. 2011; 2(5): 152-156.

[110] Bakal RL, Manwar JV, Sahare AY, Bhajipale NS, Manikrao AM. Spectrophotometric estimation of amitriptyline HCl and chlordiazepoxide in pharmaceutical dosage form. Indian Journal of Pharmaceutical Education and Research. 2008; 42: 23–26.

[111] Padgilwar SS, Manwar JV. Relative Influence of adrenergic β-agonist and antagonist on the inflammation and their interaction with aspirin. European Journal of Experimental Biology. 2013; 3(1):467-472.