

## **A REVIEW ON: DIABETES MELLITUS TREATMENT USING HERBAL DRUG**

**Pawan Prakash Mirkar\*, Shekhar S. Pandav and Dr. Gajanan S. Sanap**

Department of Pharmacy, LBYP College of Pharmacy, Pathri, Aurangabad – 431111,  
Maharashtra, India.

Article Received on  
19 Feb. 2023,

Revised on 11 March 2023,  
Accepted on 31 March 2023

DOI: 10.20959/wjpr20235-27687

### **\*Corresponding Author**

**Pawan Prakash Mirkar**

Department of Pharmacy,  
LBYP College of Pharmacy,  
Pathri, Aurangabad -  
431111, Maharashtra, India.

### **ABSTRACT**

Diabetes mellitus is one of the common metabolic problems and 2.8% of the population suffers from this disorder in the course of the world and it may cross 5.4% by the yr 2025. Oral hypoglycemic agents like sulphonylureas and biguanides are still the major players with inside the control of the disease however there is developing interest in herbal treatments because of the side outcomes related to the oral hypoglycemic agents. Herbal medicines had been the highly esteemed supply of drugs in the course of human history. They are extensively used nowadays indicating that herbs are a developing a part of modern, high-tech medicine. Diabetes mellitus is one of the maximum not common non-communicable illnesses globally. It is the fourth main

reasons of dying with inside the maximum evolved countries and there in substantial evendiced that it in epidemic in lots of developing and newly industrialized nations. This posing a severe risk to be met inside 21st century.

### **INTRODUCTION**

Diabetes mellitus is a common and really prevalent sickness affecting the residents of each developed and growing countries. It is estimated that 25% of the world population is affected by this sickness. Diabetes mellitus is because of the abnormality of carbohydrate metabolism that is related to low blood insulin level or insensitivity of target organs to insulin.<sup>[1]</sup> Despite giant development with inside the treatment of diabetes by oral hypoglycemic agents, search for newer drugs keeps due to the fact the present synthetic drugs have numerous limitations. The herbal drugs with antidiabetic activity are but to be commercially formulated as modern

drugs, even though they were acclaimed for his or her therapeutic properties with inside the traditional systems of medicinal drug.<sup>[2]</sup>

Diabetes mellitus is a systemic metabolic sickness characterized by hyperglycemia, hyperlipidemia, hyperaminoacidemia, and hypoinsulinaemia it leads to decrease in each insulin secretion and insulin action.<sup>[3]</sup> It is regularly related to the improvement of micro and macro vascular illnesses which encompass neuropathy, nephropathy, cardiovascular and cerebrovascular illnesses.<sup>[4]</sup> The sickness is related to decreased nice of life and expanded risk elements for mortality and morbidity. The long-term hyperglycemia is an essential issue with inside the improvement and development of micro- and macrovascular complications.<sup>[5]</sup>

The worldwide occurrence of diabetes for all age corporations changed into estimated to be 2.8% in 2000 and it is projected to be 5.4% in 2025. Currently available therapies for diabetes encompass insulin and numerous oral antidiabetic sellers including sulfonylureas, biguanides,  $\alpha$ -glucosidase inhibitors and glinides. In growing nations as merchandise are high priced and now no longer without problems accessible. Presently, there may be developing interest in natural treatments because of the side results related to the oral hypoglycemic agents (therapeutic agent) for the treatment of diabetes mellitus. So the conventional natural drugs are particularly used which might be received from plants, it performs essential function withinside the control of diabetes mellitus.<sup>[6]</sup> In latest years, natural drugs have began out to advantage significance as a supply of hypoglycemic sellers. Marles and Farnsworth envisioned that extra than one thousand plant species are getting used as peoples medicinal drug for diabetes<sup>[7]</sup> Biological movements of the plant merchandise used as opportunity drugs to deal with diabetes are associated with their chemical composition. Herbal merchandise or plant merchandise are wealthy in phenolic compounds, flavonoids, terpenoids, coumarins, and different ingredients which display discount in blood glucose levels.<sup>[8,9,10]</sup> Several species of natural pills were defined withinside the scientific and famous literature as having antidiabetic activity.<sup>[11]</sup> Due to their perceived effectiveness, fewer side results in clinical enjoy and comparatively low costs, herbal drugs are prescribed.<sup>[12]</sup>

### **Important medicinal plants having antidiabetic potential**

#### **Bauhinia forficata**

Bauhinia forficata is the most extensively used natural medicine for manage of diabetes in Brazil, wherein it is referred to as Pata de Vaca (cows hoof).<sup>[13]</sup> The fresh leaves are the

crucial a part of this plant which suggests the hypoglycemic activity and the genus *Bauhinia* belongs to the family *Caesalpiniaceae*.<sup>[14]</sup> The preliminary reviews of *Bauhinia forficata* antidiabetic interest in diabetic sufferers had been made by Juliani (1941)<sup>[15]</sup> and Juliani (1931).<sup>[16]</sup> According to M.T. Pepato et al (2002) *Bauhinia forficata* decoction became organized with the aid of using boiling a hundred and fifty g of sparkling leaves in 1 litre of water for five min, allowed the decoction to face for 30 min and filtered. The rats which can be used for the test had been fed a everyday laboratory chow weight loss program containing (wt./wt.) 16% protein, 66% carbohydrate and 8% fat and had been housed below a 12:12 h light: darkish cycle at 22-25°C. In this test they divided the rats into groups i.e., diabetic and non diabetic businesses, accompanied by administered the streptozotocin (STZ) forty mg/kg body weight, after three days the serum and urinary glucose degrees had been increased. Then one organization became injected with *Bauhinia forficata* decoction and every other with the drinking-water as manage organization. After 31 days of remedy the diabetic organization treated with decoction confirmed a massive discount in plasma glucose and urinary glucose. So the pharmacological, biochemical, histological and chemical research are needed to elucidate the precise mechanism of action of *Bauhinia forficata* leaf decoction and to isolate any active compounds. Such investigations need to additionally be carried out concerning type 2 diabetes.<sup>[17]</sup>

### ***Ricinus communis***

*Ricinus communis* is the conventional medicine which was used for the control of Diabetes mellitus. It is known as as Erandah in Sanskrit, Amudam in Telugu and Arandi in Hindi and is also called castor oil. It belongs to the family *Euphorbiaceae*, and it changed into cultivated throughout India for getting its seed oil. Castor oil were utilized in classical Egyptian and Greek remedy and their use has been defined withinside the *Susruta* and *Ayurveda* as early as 6th century B.C.<sup>[18]</sup> In the Indian device of remedy, the leaf, root and seed oil of this plant were used for the treatment of inflammation and liver disorders.<sup>[19]</sup> Fifty percent of ethanolic extract of the root, stem and leaves of this plant confirmed hypoglycemic interest in everyday animals and antihyperglycemic interest in diabetic animals in initial screening studies.<sup>[20]</sup> The Administration of the ethanolic extract for an extended period led to a considerable diminution of Blood Glucose withinside the diabetic rats, while there was no significant alteration withinside the Blood Glucose of the control animals.<sup>[21]</sup>

**Combretum micranthum**

Combretum Micranthum is a medicinal plant used for treating diabetes in Northwestern Nigeria. It is normally recognised as ‘geza’ in Hausa, belong to the family of Combretaceae. It is a widely known ethno medicinal plant utilized in West Africa for treating numerous diseases.<sup>[22,23]</sup> In Nigeria, greater than 80% of the people rely upon herbal drug treatments for treating their illnesses.<sup>[24]</sup> The plant have additionally been documented to show antioxidant, antimicrobia<sup>[25]</sup> as well as antiinflammatory<sup>[26]</sup> properties. The Aqueous extract of Combretum Micranthum turned into organized through using Soxhlet extractor and it turned into dried in an evaporator at 45°C and stored at 4°C till ready for use. The hypoglycemic activity of this plant extract turned into examined through using glucose tolerance test and fasting blood sugar assessment in normal rats. The antihyperglycemic capacity of this plant turned into done through taking organization of animals i.e., diabetic group and nondiabetic groups.

**Swertia punicea**

Swertia plants are maximum broadly used traditional drugs withinside the treatment of diabetes.<sup>[27]</sup> The entire plant of Swertia punicea (5.6 kg) turned into extracted with 90% Ethanol at room temperature to obtain 940 g of crude extract, which was handled successively with petroleum ether, EtOAc, and n-butanol. It belongs to the family Gentianaceae. Some plant extracts and xanthonoids, the predominant elegance of compounds some of the chemical ingredients of this genus, were stated to show significantly hypoglycemic activities.<sup>[28]</sup> According to the Pen and Fang (2003) research the plant Swertia Punicea suggests a great hypoglycemic activity in alloxan-precipitated diabetic mice,<sup>[29]</sup> and might lessen oxidative injury in diabetic mice.<sup>[30]</sup> In addition, the Ethanol extracts and Ethyl acetate soluble fraction of Swertia Punicea confirmed hypoglycemic effects in STZ-induced type-2 diabetic mice and can be beneficial to development of insulin resistance (IR).<sup>[31]</sup>

**Sarcopoterium spinosum**

Sarcopoterium spinosum species is a common medicinal plant withinside the Mediterranean region, and it is extensively used as an antidiabetic drug by Bedouin healers. The ethnobotanical surveys stated as a medicinal plant, utilized by conventional Arab and Bedouin medicinal drug for the control of diabetes, digestive problems, pain relief or cancer. It is likewise called thorny burnet (syn: Poterium spinosum L.; in Hebrew, “sira kotsanit”, in arabic, “natsh” or “bilan”)<sup>[32,33]</sup> is an plentiful and function species of the semi-steppe shrublands (phrygana) and Batha of the Eastern Mediterranean region. The plant

*Sarcopoterium spinosum* is a chamaephyte of the Rosaceae family.<sup>[34]</sup> Dafni et al. had been examined that the basis extract of this plant changed into used for treating diabetes in Muslim folk medicine<sup>[35]</sup> and a completely few research have confirmed this facts and measured its antidiabetic activity. In the past due 1960s and 1980s, numerous studies had been executed to show the root extract of *Sarcopoterium spinosum* exhibits a hypoglycemic impact in rats.<sup>[36]</sup>

### ***Brassica juncea***

It is normally used spice in diverse food objects in Tamilnadu. *B. juncea* is a conventional medicinal plant which belongs to family Cruciferae. *B. juncea* aqueous seed extract has a amazing hypoglycemic activity which became investigated in STZ brought on diabetic male albino rat. Doses that have hypoglycemic activity became reported as 250, 350, 450 mg/kg.<sup>[37]</sup>

### ***Eugenia jambolan***

*Eugenia jambolana* (*E. jambolana*) popularly called Jamun or Indian blackberry has been indicated in Ayurveda, an historical system of Indian medicine, to be used in DM. In accordance to its claimed anti-diabetic impact in conventional medicine, *E. jambolana* has been pronounced to have hypoglycemic results each in experimental models and medical studies.<sup>[38]</sup>

### ***Coccinia grandis***

Hypoglycemic activity changed into evaluated in alcoholic extracts of *Coccinia grandis* (*C. grandis*) leaves. Alcoholic extract 600 mg/kg bw changed into injected orally to mice. Oral management of alcoholic extract of leaves of *C. grandis* confirmed substantial hypoglycemic effect on blood glucose level in regular fasted rats.<sup>[39]</sup>

### ***Allium sativum* L. (garlic): (Liliaceae)**

It is a perennial herb cultivated throughout India. Oral management of the garlic extract significantly decreases serum glucose, overall cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels, while will increase serum insulin in diabetic rats however not in regular rats when in comparison with antidiabetic drug glibenclamide. The antidiabetic impact of the extract changed into greater effective than glibenclamide. It is concluded that the plant must be considered as excellent candidate for destiny research on diabetes mellitus.<sup>[40]</sup>

### Herbal Drug Formulations

Diabecon synthetic by 'Himalaya' is said to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells restore and regeneration and increase c peptide level. It has antioxidant properties and protects B cells from oxidative stress. It exerts an insulin like movement by decreasing the glycated haemoglobin levels, normalizing the microalbuminurea and modulating the lipid profile. It minimizes long time diabetic complications.<sup>[41]</sup>

Epinsulin advertised by Swastik formulations, incorporates epicatechin, a benzopyran, as an active principle. Epicatechin increases the cAMP content material of the islet, which is related to expanded insulin release. It performs a function withinside the conversion of proinsulin to insulin by growing cathepsin activity. Additionally it has an insulin-mimetic impact on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient's erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It keeps the integrity of all organ systems affected by the disease. It is stated to be a healing for diabetes, Non Insulin Dependant Diabetes Mellitus (NIDDM) and a great adjuvant for Insulin Dependant Diabetes Mellitus (IDDM), in order to lessen the quantity of needed insulin. It is counseled together with current oral hypoglycemic drugs. And is known to prevent diabetic complication. It has mild hypoglycemic activity and subsequently induces no threat of being hypoglycemic. Pancreatic Tonic (ayurvedic herbal supplement): Pancreas Tonic is a botanical aggregate of conventional Indian Ayurvedic herbs presently to be had as a nutritional supplement.

Bitter gourd powder advertised by Garry and Sun. It lowers blood & urine sugar levels. It will increase body's resistance in opposition to infections and purifies blood. Bitter Gourd has wonderful medicinal virtues. It is antidotal, antipyretic tonic, appetizing, stomachic, antibilious and laxative. The sour Gourd is likewise utilized in local drug treatments of Asia and Africa. The Bitter gourd is mainly used as a peoples remedy for diabetes. It carries compounds like sour glycosides, saponins, alkaloids, decreasing sugars, phenolics, oils, unfastened acids, polypeptides, sterols, 17-amino acids together with methionine and a crystalline product named p-insulin. It is said to have hypoglycemic hobby similarly to being antihaemorrhoidal, astringent, stomachic, emmenagogue, hepatic stimulant, anthelmintic and blood cleanser Dia-Care synthetic by Admark Herbals Ltd. is said to be powerful for each Type 1, Type 2 diabetes inside ninety days of remedy and treatment plans inside 18 months.

Persons taking insulin will ultimately be liberated from the dependence on it. The complete treatment completes in 6 phases, each section being of 90 days. Approx. 5 grams (1 tea spoon) powder is mixed with half of glass of water, stirred properly and saved overnight. Only the water and now no longer the sediment must be taken withinside the morning on empty stomach. To the ultimate medicine clean water is brought and saved for the complete day and is consumed 1/2 of an hour earlier than dinner. The flavor of the drug is very sour. It is a pure natural components with none side effects.<sup>[42]</sup>

Diabetes-Daily Care manufactured through Nature's Health Supply is a Unique, Natural Formula, which successfully and accurately Improves Sugar Metabolism. Diabetes Daily Care™ turned into formulated for type 2 diabetics and carries all herbal substances listed in Table 1 in the proportion most appropriate for the body's use. Gurmar powder synthetic through Garry and Sun is an anti-diabetic drug, which suppresses the intestinal absorption of sacharides, which prevents blood sugar fluctuations. It additionally correlates the metabolic activities of liver, kidney and muscle tissues. Gurmar stimulates insulin secretion and has blood sugar lowering properties. It blocks sweet flavor receptors while carried out to tongue in diabetes to put off glycosuria. It deadens flavor of goodies and sour such things as quinine (consequences lasts for 1 to two hours). Besides having those properties, it's far a cardiac stimulant and diuretic and corrects metabolic sports of liver, kidney and muscle tissues DIABETA, a system of Ayurvedic Cure, to be had withinside the capsule shape is an anti-diabetic with mixture of confirmed anti-diabetic fortified with powerful immunomodulators, antihyperlipidemics, anti-pressure and hepatoprotective of plant origin. The system of Diabeta is primarily based totally on historic ayurvedic references, similarly corroborated via current studies and scientific trials. Diabeta acts on one-of-a-kind webweb sites in differing methods to successfully manage elements and pathways main to diabetes mellitus. It assaults the diverse elements, which precipitate the diabetic condition, and corrects the degenerative complications, which end result because of diabetes.<sup>[43]</sup>

Diabeta is secure and effective in coping with Diabetes Mellitus as a single agent complement to synthetic anti-diabetic tablets. Diabeta enables overcome resistance to oral hypoglycemic drugs whilst used as adjuvant to instances of out of control diabetes. Diabeta confers a feel of well-being in sufferers and promotes symptomatic relief of complaints like weak point giddiness, pain in legs, body ache, polyuria and pruritis. Syndrex synthetic through Plethico Laboratory carries extracts of germinated fenugreek seed. Fenugreek is used



as an component of conventional formulations over a thousand years. We are presently studying the mechanism of this antidiabetic drug using animal version on one hand and cultured islet cells at the other. Thus many different flora had been used personally or in formulations for treatment of diabetes and its complications. One of the main troubles with this natural system is that the active elements aren't properly defined. It is crucial to recognise the active aspect and their molecular interaction, which will assist to examine therapeutic efficacy of the product and additionally to standardize the product. Efforts are now being made to research mechanism of motion of some of those flora using version systems.<sup>[43]</sup>

**Table 1: Formulated Herbal Drugs with antidiabetic properties.**

Drug	Company	Ingredients
Diabecon	Himalaya	<i>Gymnema sylvestre</i> , <i>Pterocarpus marsupium</i> , <i>Glycyrrhiza glabra</i> , <i>Casearia esculenta</i> , <i>Syzygium cumini</i> , <i>Asparagus racemosus</i> , <i>Boerhavia diffusa</i> , <i>Sphaeranthus indicus</i> , <i>Tinospora cordifolia</i> , <i>Swertia chirata</i> , <i>Tribulus terrestris</i> , <i>Phyllanthus amarus</i> , <i>Gmelina arborea</i> , <i>Gossypium herbaceum</i> , <i>Berberis aristata</i> , <i>Aloe vera</i> , <i>Triphala</i> , <i>Commiphora wightii</i> , shilajeet, <i>Momordica charantia</i> , <i>Piper nigrum</i> , <i>Ocimum sanctum</i> , <i>Abutilon indicum</i> , <i>Curcuma longa</i> , <i>Rumex maritimus</i>
Diasulin		<i>Cassia auriculata</i> , <i>Coccinia indica</i> , <i>Curcuma longa</i> , <i>Emblica officinalis</i> , <i>Gymnema sylvestre</i> , <i>Momordica charantia</i> , <i>Scoparia dulcis</i> , <i>Syzygium cumini</i> , <i>Tinospora cordifolia</i> , <i>Trigonella foenum graecum</i>
Pancreatic tonic 180 cp	ayurvedic herbal supplement	<i>Pterocarpus marsupium</i> , <i>Gymnema sylvestre</i> , <i>Momordica charantia</i> , <i>Syzygium cumini</i> , <i>Trigonella foenum graecum</i> , <i>Azadirachta indica</i> , <i>Ficus racemosa</i> , <i>Aegle marmelos</i> , <i>Cinnamomum tamala</i>
Ayurveda alternative herbal formula to Diabetes:	Chakrapani Ayurveda	Gurmar ( <i>Gymnema sylvestre</i> ) Karela ( <i>Momordica charantia</i> ) Pushkarmool ( <i>Inula racemosa</i> ) Jamun Gutli ( <i>Syzygium cumini</i> ) Neem ( <i>Azadirachta indica</i> ) Methika ( <i>Trigonella foenum graecum</i> ) Guduchi ( <i>Tinospora cordifolia</i> )
Bitter gourd Powder	Garry and Sun natural Remedies	Bitter gourd ( <i>Momordica charantia</i> )
Dia-care	Admark Herbals Limited	Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal.
Diabetes-Daily Care	Nature's Health Supply	Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, <i>Gymnema sylvestre</i> 25% extract <i>Momordica</i> 7% extract, Licorice Root 20% extract
Gurmar powder	Garry and Sun natural Remedies	Gurmar ( <i>Gymnema sylvestre</i> )
Epinsulin	Swastik Formulations	vijaysar ( <i>Pterocarpus marsupium</i> )
Diabecure	Nature beaute sante	<i>Juglans regia</i> , <i>Berberis vulgaris</i> , <i>Erythraea centaurium</i> , <i>Millefolium</i> , <i>Taraxacum</i>
Diabeta	Ayurvedic cure Ayurvedic Herbal Health Products	<i>Gymnema sylvestre</i> , <i>Vinca rosea</i> (Periwinkle), <i>Curcuma longa</i> (Turmeric), <i>Azadirachta indica</i> (Neem), <i>Pterocarpus marsupium</i> (Kino Tree), <i>Momordica charantia</i> (Bitter Gourd), <i>Syzygium cumini</i> (Black Plum), <i>Acacia arabica</i> (Black Babhul), <i>Tinospora cordifolia</i> , <i>Zingiber officinale</i> (Ginger)
Syndrex	Plethico Laboretaries	Germinated Fenugreek seed extract

## DISCUSSION

The use of herbs is not a new trouble as herbs have been recognised for a long term and were utilized by many humans to deal with a variety of diseases. Doctors will want to hold track of this exercise and that they want to recognize greater as regards to herbs as they will enhance



or worsen the final results of treatment in their patients. Diabetes is one circumstance wherein herbs are often given as they're expected to have a main function within the treatment of the disease. The present study has shown that 17.4% of the diabetic patients had used herbs within the last year. The actual percent can be greater than that if the length of the study of natural use become prolonged for greater than a year. Most of those patients had listed loads of herbs for the treatment in their diseases however few patients have been frequently using them. About one-third could abstain from the usage of clinical treatment once they were the usage of the herbs. The popularity of the herbs for the treatment of sufferers with chronic sicknesses can be attributed to the long-standing struggling of the sufferers or failure of the clinical treatment to carry a short and long-lasting relief. The maximum common forms of herbs used amongst our sufferers have been myrrh, black seed, helteet and fenugreek. In every other take a look at which become performed on American patient's of Mexican origin<sup>1</sup> the maximum common herbs. used have been Nopal and Aloe Vera. In Morocco, fenugreek become the primary within the top 10 maximum encouraged antidiabetic plants even as in Quebec, Canada, blueberry become the herb maximum often used. This variant can be associated with the supply of those herbs in sure groups than others and additionally tradition and conduct can also additionally play a role of their choice. Patients who took the herbs in step with a friend's recommendation in this take a look at were 42% and this may draw interest to the significance of health education to the community. If they have been nicely informed this is probably reflected within the type of recommendation, they had given. Education concerning the use of herbs is a great area to be tackled within the field of fitness training. Proper fitness training also can persuade a better percent of diabetic patients to inform their medical doctors concerning their use of herbs. Indeed, the existing study indicates that 73% of herbs customers did not tell their health practitioner concerning it. Although 49% of herbs customers are not glad with it however nevertheless lots of them intend to apply them again. The reuse of herbs can be influenced by anxiety, as a number of them stated or could be because of a friends advice.

## CONCLUSION

Diabetes mellitus is a most common endocrine disorder, affecting extra than 300million people worldwide. For this, remedies evolved alongside the concepts of western medicine (allopathic) are regularly limited in efficacy, bring the chance of adverse effects, and are regularly too costly, mainly for the growing world. Therefore, treating diabetes mellitus with plant derived compounds that are reachable and do not require exhausting pharmaceutical

synthesis appears exceptionally appealing to folklore medicinal plants for the treatment of Diabetes mellitus. Folklore medicinal plants are in most cases used for rural areas; because the provision of lavish quantity of medicinal plants the ones areas. Therefore, treating diabetes mellitus with plant derived compounds that are accessible and do not require exhausting pharmaceutical synthesis appears exceptionally attractive.

### ACKNOWLEDGEMENT

I would like to express my genuine thanks Dr. Gajanan Sanap, Principal, LBYP college of Pharmacy, for giving me this opportunity to carry out my study in the LBYP (Affiliated University DBATU) Maharashtra, India.

### REFERENCE

1. Gordon AE, Shaughnessy AF. Saw palmetto for prostate disorders. American family physician, Mar. 15, 2003; 67(6): 1281-3.
2. Zeiger E, Tice R. Saw palmetto (*Serenoa repens*) and one of its constituent sterols-sitosterol. Review of toxicological literature, Nov, 1997.
3. Bach D, Ebeling L. Long-term drug treatment of benign prostatic hyperplasia—results of a prospective 3-year multicenter study using Sabal extract IDS 89. Phytomedicine, Sep. 1, 1996; 3(2): 105-11.
4. Gerber GS. Saw palmetto for the treatment of men with lower urinary tract symptoms. The Journal of urology, May. 1, 2000; 163(5): 1408-12.
5. Wilt TJ, Ishani A, Stark G, MacDonald R, Lau J, Mulrow C. Saw palmetto extracts for treatment of benign prostatic hyperplasia: a systematic review. Jama, Nov. 11, 1998; 280(18): 1604-9.
6. Booker A, Suter A, Krnjic A, Strassel B, Zloh M, Said M, Heinrich M. A phytochemical comparison of saw palmetto products using gas chromatography and <sup>1</sup>H nuclear magnetic resonance spectroscopy metabolomic profiling. Journal of Pharmacy and Pharmacology, Jun, 2014; 66(6): 811-22.
7. Chatterjee S, Agrawala SK. Saw palmetto (*Serenoa repens*) in androgenic alopecia An effective phytotherapy.
8. Iehlé C, Délos S, Guirou O, Tate R, Raynaud JP, Martin PM. Human prostatic steroid 5 $\alpha$ -reductase isoforms—A comparative study of selective inhibitors. The Journal of Steroid Biochemistry and Molecular Biology, Sep. 1, 1995; 54(5-6): 273-9.

9. Sultan C, Terraza A, Devillier C, Carilla E, Briley M, Loire C, Descomps B. Inhibition of androgen metabolism and binding by a liposterolic extract of “*Serenoa repens* B” in human foreskin fibroblasts. *Journal of steroid biochemistry*, Jan. 1, 1984; 20(1): 515-9.
10. Liang T, Liao S. Inhibition of steroid 5  $\alpha$ -reductase by specific aliphatic unsaturated fatty acids. *Biochemical Journal*, Jul. 15, 1992; 285(2): 557-62.
11. Sargent NS, Habib FK. Partial purification of human prostatic 5 $\alpha$ -reductase (3-oxo-5 $\alpha$ -steroid: NADP+ 4-ene-oxido-reductase; EC 1.3. 1.22) in a stable and active form. *The Journal of Steroid Biochemistry and Molecular Biology*, Jan. 1, 1991; 38(1): 73-7.
12. Strauch G, Perles P, Vergult G, Gabriel M, Gibelin B, Cummings S, Malbecq W, Malice MP. Comparison of finasteride (Proscar®) and *Serenoa repens* (Permixon®) in the inhibition of 5-alpha reductase in healthy male volunteers. *European urology*, 1994; 26: 247-52.
13. Carraro JC, Raynaud JP, Koch G, Chisholm GD, Di Silverio F, Teillac P, Da Silva FC, Cauquil J, Chopin DK, Hamdy FC, Hanus M. Comparison of phytotherapy (Permixon®) with finasteride in the treatment of benign prostate hyperplasia: a randomized international study of 1,098 patients. *The Prostate*, Oct, 1996; 29(4): 231-40.
14. Dedhia RC, McVary KT. Phytotherapy for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *The Journal of urology*, Jun. 1, 2008; 179(6): 2119-25.
15. Tacklind J, MacDonald R, Rutks I, Stanke JU, Wilt TJ. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database of Systematic Reviews*, 2009; 2.
16. Agbabiaka TB, Pittler MH, Wider B, Ernst E. *Serenoa repens* (Saw Palmetto) A Systematic Review of Adverse Events. *Drug safety*, Aug, 2009; 32: 637-47.
17. Markowitz JS, Donovan JL, DeVane CL, Taylor RM, Ruan Y, Wang JS, Chavin KD. Multiple doses of saw palmetto (*Serenoa repens*) did not alter cytochrome P450 2D6 and 3A4 activity in normal volunteers. *Clinical Pharmacology & Therapeutics*, Dec, 2003; 74(6): 536-42.
18. Morganti P, Fabrizi G, James B, Bruno C. EFFECT OF GELATIN-CYSTINE ANO SERENOA REPENS EXTRACT ON FREE RAOICALS LEVEL ANO HAIR GROWTH. *J Appl Cosmetol*, Jul, 1998; 16: 57-64.
19. Prager N, Bickett K, French N, Marcovici G. A randomized, double-blind, placebo-controlled trial to determine the effectiveness of botanically derived inhibitors of 5- $\alpha$ -reductase in the treatment of androgenetic alopecia. *Journal of Alternative & Complementary Medicine*, Apr 1, 2002; 8(2): 143-52.

20. Rossi A, Mari E, Scarno M, Garelli V, Maxia C, Scali E, Iorio A, Carlesimo M. Comparative effectiveness and finasteride vs serenoa repens in male androgenetic alopecia: a two-year study. *International Journal of Immunopathology and Pharmacology*, Oct, 2012; 25(4): 1167-73.
21. Narda M, Aladren S, Cestone E, Nobile V. Efficacy and safety of a food supplement containing L-cystine, Serenoa repens extract and biotin for hair loss in healthy males and females. A prospective, randomized, double-blinded, controlled clinical trial. *J Cosmo Trichol.*, 2017; 3(127): 2.
22. Morabito P, Miroddi M, Giovinazzo S, Spina E, Calapai G. Serenoa repens as an endocrine disruptor in a 10-year-old young girl: a new case report. *Pharmacology*, 2015; 96(1-2): 41-3.
23. Gómez Grau E, Lladós Sevilla M, Mira J, Vivancos F. Eficacia de un complemento alimenticio con serenoa serrulata y tocotrienol-tocoferol frente a la alopecia androgenética y el efluvio telógeno femeninos: a propósito de un estudio piloto. *Revista argentina de dermatología*, Mar, 2015; 96(1): 43-55.
24. Zanzottera F, Bizzaro G, Michelotti A, Nobile V. Efficacy of a nutritional supplement, standardized in fatty acids and phytosterols, on hair loss and hair health in both women and men. *J Cosmo Trichol*, 2017; 3(121): 2.
25. Pezza M, Carlomagno V, Casucci G. Telogen effluvium treated with Serenoa repens supplement. *Senses and Sciences*, Mar 27, 2014; 1(1).
26. Murugusundram S. Serenoa repens: does it have any role in the management of androgenetic alopecia?. *Journal of cutaneous and aesthetic surgery*, Jan, 2009; 2(1): 31.
27. Togni S, Maramaldi G, Meneghin M, Giacomelli L, Eggenhoffner R. Effective oral treatment for scalp disorders: results from a double blind, placebo-controlled study. *Esperienze Dermatol*, 2016; 8: 187-91.
28. Dobrev H. Clinical and instrumental study of the efficacy of a new sebum control cream. *Journal of cosmetic dermatology*, Jun, 2007; 6(2): 113-8.
29. Strzelecka H, Kowalski J, editors. *Encyklopedia zielarstwa i ziołolecznictwa*. Wydawn. Naukowe PWN, 2000.
30. Wilt TJ, Ishani A, Rutks I, MacDonald R. Phytotherapy for benign prostatic hyperplasia. *Public health nutrition*, Dec, 2000; 3(4a): 459-72.
31. Zaman F, Bach C, Junaid I, Papatsoris AG, Pati J, Masood J, Buchholz N. The floppy iris syndrome—what urologists and ophthalmologists need to know. *Current Urology*, 2012; 6(1): 1-7.

32. Tsatsos M, MacGregor C, Athanasiadis I, Moschos M, Mataftsi A, Ziakas N. Phytotherapy and intraoperative floppy iris syndrome: the implications. *Eye.*, Jun, 2017; 31(6): 823-6.
33. Neff KD, Sandoval HP, de Castro LE, Nowacki AS, Vroman DT, Solomon KD. Factors associated with intraoperative floppy iris syndrome. *Ophthalmology*, Apr. 1, 2009; 116(4): 658-63.
34. Yeu E, Grostern R. Saw palmetto and intraoperative floppy-iris syndrome. *Journal of Cataract & Refractive Surgery*, May. 1, 2007; 33(5): 927-8.
35. Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. In *Seminars in integrative medicine*, Jun. 1, 2004; 2(2): 54-71). WB Saunders.
36. Raman P, DeWitt DL, Nair MG. Lipid peroxidation and cyclooxygenase enzyme inhibitory activities of acidic aqueous extracts of some dietary supplements. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, Feb, 2008; 22(2): 204-12.
37. Goldmann WH, Sharma AL, Currier SJ, Johnston PD, Rana A, Sharma CP. Saw palmetto berry extract inhibits cell growth and Cox-2 expression in prostatic cancer cells. *Cell Biology International*, Nov 1, 2001; 25(11): 1117-24.
38. Tan HY, San-Marina S, Wang N, Hong M, Li S, Li L, Cheung F, Wen XY, Feng Y. Preclinical models for investigation of herbal medicines in liver diseases: Update and perspective. *Evidence-Based Complementary and Alternative Medicine*, Jan. 1, 2016; 2016.
39. Reid EE, Haley AC, Borovicka JH, Rademaker A, West DP, Colavincenzo M, Wickless H. Clinical severity does not reliably predict quality of life in women with alopecia areata, telogen effluvium, or androgenic alopecia. *Journal of the American Academy of Dermatology*, Mar. 1, 2012; 66(3): e97-102.
40. Schmitt JV, Ribeiro CF, Souza FH, Siqueira EB, Bebbber FR. Hair loss perception and symptoms of depression in female outpatients attending a general dermatology clinic. *Anais brasileiros de dermatologia*, 2012; 87: 412-7.
41. Grimalt R. Psychological aspects of hair disease. *Journal of Cosmetic Dermatology*, Jun, 2005; 4(2): 142-7.
42. Rogers NE, Avram MR. Medical treatments for male and female pattern hair loss. *Journal of the American Academy of Dermatology*, Oct 1, 2008; 59(4): 547-66.

43. Lourith N, Kanlayavattanakul M. Hair loss and herbs for treatment. Journal of cosmetic dermatology, Sep, 2013; 12(3): 210-22.