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## A review on levodopa and beta-sitosterol and its pharmacological actions in *Bauhinia racemosa*, *Canavalia gladiata*, *Vigna vexillata* medicinal plants

**Shardul S Kulkarni, Ratnakar B Lanjewar and Sunita M Gadegone**

### Abstract

Healing with medicinal plants is as old as mankind itself. The connection between man and his search for drugs in nature dates from the far past, of which there is ample evidence from various sources: written documents, preserved monuments, and even original plant medicines. In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and lesser side effects. Based on current research and financial investments, medicinal plants will seemingly, continue to play an important role as a health aid.

The use of Ayurvedic medicines is common in both adults and children and is increasing in many areas of the world. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. This paper will discuss the benefits with use of levodopa and beta-sitosterol. The current review focuses on uses of Levodopa and Beta-sitosterol and medicinal plants which contain levodopa and beta-sitosterol. *Bauhinia racemosa*, *Canavalia Gladiata*, *Vigna vexillata* contains many phyto-constituents so there is major scope for phyto-constituents analysis of this underutilised plants.

**Keywords:** Levodopa, beta-sitosterol, *Bauhinia racemosa*, *Canavalia gladiata*, *Vigna vexillata*

### Introduction

Awareness of medicinal plants usage is a result of the many years of struggles against illnesses due to which man learned to pursue drugs in barks, seeds, fruit bodies, and other parts of the plants. Contemporary science has acknowledged their active action, and it has included in modern pharmacotherapy a range of drugs of plant origin, known by ancient civilizations and used throughout the millennia. The knowledge of the development of ideas related to the usage of medicinal plants as well as the evolution of awareness has increased the ability of many vaidya and experts in pharmacy [1]. Healing with medicinal plants is as old as mankind itself. The connection between man and his search for drugs in nature dates from the far past, of which there is ample evidence from various sources: written documents, preserved monuments, and even original plant medicines [1].

There are many traditional systems of medicine in the world, each with different associated philosophies and cultural origins [2]. India is the largest producer of medicinal herbs and is called as botanical garden of the world. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. Ayurveda is the most widely practised of the Indian traditional medicine systems. Siddha and unani medicinal systems are also used in Indian subcontinent [4]. Many traditional medicinal systems localised in there region only such as Tibetan traditional medicine and few traditional medicinal systems like Ayurveda and Chinese medicine are famous and used worldwide [4].

### Importants of Phyto-Constituents

Phytochemicals or phytoconstituents (from the Greek word phyto, meaning plant) are biologically active, naturally occurring chemical compounds found in plants, which provide health benefits for humans further than those attributed to macronutrients and micronutrients [5]. They protect plants from disease and damage and contribute to the plant's color, aroma and flavor. In general, the plant chemicals that protect plant cells from environmental hazards such

As pollution, stress, drought, UV exposure and pathogenic attack are called as phytochemicals or phytoconstituents [6-7]. Recently, it is clearly known that they have roles in the protection of human health, when their dietary intake is significant. More than 4,000 phytochemicals have been cataloged [8] and are classified by protective function, physical characteristics and chemical characteristics [9] and About 150 phytochemicals have been studied in detail [10].

Medicinal plants contain many chemical compounds which are the major source of therapeutic agents to cure human diseases [11]. Plant contains alkaloids, flavonoids, glycosides, tannins, saponins, phenolics and terpenoids which shows in image-1 and Image 2 shows approximate percentage of phytoconstituents [12]. Phytochemicals accumulate in different parts of the plants, such as in the roots, stems, leaves, flowers, fruits or seeds [13]. Many phytochemicals, particularly the pigment molecules, are often concentrated in the outer layers of the various plant tissues. Levels vary from plant to plant depending upon the variety, processing, cooking and growing conditions [14]. Phytochemicals are also available in supplementary forms, but evidence is lacking that they provide the same health benefits as dietary phytochemicals [15]. These compounds are known as secondary plant metabolites and have biological properties such as antioxidant activity, antimicrobial effect, modulation of detoxification enzymes, stimulation of the immune system, decrease of platelet aggregation and modulation of hormone metabolism and anticancer property.

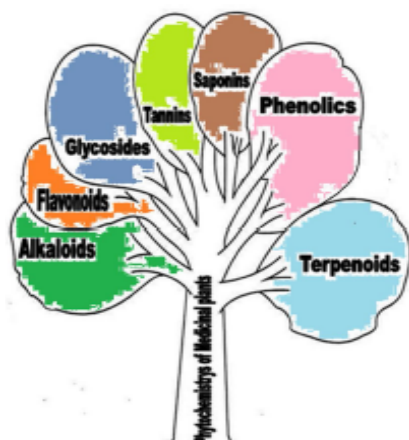


Image 1: Phytochemistry of medicinal plants.

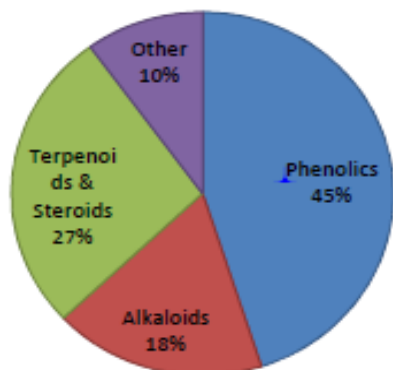


Image 2- Pie chart representing the major groups of plant Phytochemicals

Many traditional medicines in use are derived from medicinal plants, minerals and organic matter eg. euginol, gallic acid,

ascorbic acid, beta-sitosterol, levodopa etc. Various medicinal plants like neem, Arjuna, aswagandha, tulsi, jambhul etc. traditionally used for treatment. Many plants contain betasitosterol and levodopa eg. Bakala, halunda, apata, abai, kanchan, vilayati babul.

Levodopa or L-DOPA (3, 4-dihydroxy-L-phenylalanine) is an intermediate in dopamine biosynthesis. Medications can help manage problems with walking, movement and tremor by increasing the brain's supply of dopamine. The most effective Parkinson's drug is L-DOPA, it passes into the brain and is converted to dopamine. L-DOPA is used as a prodrug to increase dopamine levels for the treatment of Parkinson's disease, since it is able to cross the blood-brain barrier whereas dopamine itself cannot. Once L-DOPA has entered the central nervous system, it is metabolized to dopamine by aromatic L-amino acid decarboxylase [7].

The initial enzymatic reaction in the biosynthesis of brain catechol amines involves the formation of the catechol amino acid Ldihydroxyphenylalanine (L-DOPA) from tyrosine. Once formed, the L-DOPA is immediately decarboxylated to form dopamine, which in some neurons, is further transformed to norepinephrine [8].

L-DOPA cannot be detected normally in the brain or in the blood, and thus it is unlikely that circulating L-DOPA is a physiological precursor for brain catecholamines. However, when exogenous L-DOPA is administered to experimental animals, the concentration of dopamine in the brain increase [9]. L-DOPA is combined with carbidopa to create the combination drug Sinemet in Europe and L-DOPA is combined with a similar substance, benserazide [6]. In prolonged L-DOPA therapy, the apparent buffering capacity is lost and the patient's motor state may fluctuate dramatically with each dose of the drug, a common problem is the development of wearing off phenomenon: each dose of L-DOPA affectively improves mobility for a period of time, about 1 or 2 hours, but rigidity and akinesia return rapidly at the end of dosing interval [10].

It is relatively high demand and spiralling price in the market, demands for a suitable method to be standardized to control amount of L-dopa in the finished product. Phytochemical evaluation is one of the tools for the quality assessment, which includes preliminary phytochemical screening, chemoprofiling and marker compound analysis using modern analytical techniques. The British Pharmacopoeia describes a nonaqueous titration for the determination of L-dopa [11].

The United States Pharmacopoeia recommends a non-aqueous titrimetric procedure with potentiometric end point determination of L-dopa and extractive procedure followed by UV assay for its determination in formulations [12]. Parikh *et al.* described high performance liquid chromatography method for estimation of L-dopa in plant [13]. Siddhuraju *et al.* developed a rapid reversed-phase high performance liquid chromatographic method for the quantification of L-dopa, non-methylated and methylated tetrahydroisoquinoline compounds from Mucunabeans [14]. A quantitative estimation of L-dopa in tablets has been reported by high performance thin layer chromatography method [15-16].

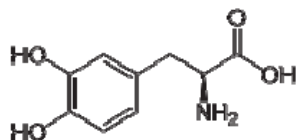
Plant sterols are steroid alcohols. Phyto-sterols regulate the membrane properties of the plant cells and participate in the control of membrane-associated metabolic processes. Sterols also play an important role in cellular and developmental processes in plants as precursors of brassi- nosteroids. They also act as substrates for a wide variety of secondary metabolites such as the glycoalkaloids, saponins. A major function of phytosterols in diet is the inhibition of absorption

and subsequent compensatory stimulation of the synthesis of cholesterol. They are generally regarded as a kind of functional factor which could lower serum cholesterol and LDL-C level. Among different kinds of phytosterols,  $\beta$ -sitosterol has the most powerful serum cholesterol-lowering effect. Phytosterols are made up of a tetracyclic cyclopenta [ $\alpha$ ] phenanthrene ring and a long flexible side chain at the C-17 carbon atom. The four rings (A, B, C, D, from left to right) have trans ring junctures, forming a flat  $\alpha$  system. The most common representatives are sitosterol, stigmasterol and campesterol (4-desmethyl sterol). Campesterol and sitosterol have a  $\Delta^5$  double bond and an additional Sitosterol is the principal sterol in plant materials. Generally it refers to beta-sitosterol which has  $\Delta^5$  double bond and  $\alpha$ -ethyl at C-24 [17-18]. Beta-sitosterol is a main phyto-sterol found in numerous plants including rice, wheat, corn, nut, peanut etc. It is structurally related to cholesterol [19-20]. beta-sitosterol has recorded an amazing health benefits as an hepatoprotective [21], antioxidant and antipyretic [22-23], inflammatory disorders and rheumatoid arthritis [24], colon cancer [25], benign prostatic hypertrophy [26-27] and breast cancer [28]. Preliminary phytochemical screening, TLC fingerprinting and co-TLC studies (with beta-sitosterol) of Acacia barks revealed the presence of with beta-sitosterol and an identical spot as that of standard beta -sitosterol was observed. Further it was confirmed by  $R_f$  values comparison and multi wavelength scanning.

Previously, Lembcke *et al.* has been quantified beta-sitosterol by liquid chromatography and tandem mass spectrometry using atmospheric pressure photo-ionization (APPI- LC-MS-MS) [29]. Nair *et al.* quantified by using liquid chromatography (LC) with evaporative light scattering detection (ELSD) [30]. kamm *et al.* quantified using online liquid chromatography-gas chromatography (LC-GC) [31] and Sorenson *et al.* using gas chromatography [32].

### General Profile of Standard Levodopa and Beta-Sitosterol

Levodopa-  
Structure:



IUPAC name: (S)-2-Amino-3-(3, 4- dihydroxyphenyl) propanoic acid

Molecular formula:  $C_9H_{11}NO_4$

Molecular weight: 197

Appearance: white crystalline powder

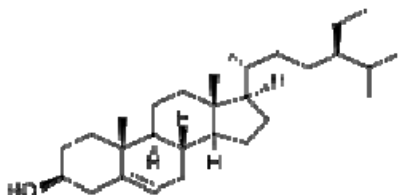
Solubility: Soluble in water, Partially insoluble in ethanol and insoluble chloroform acetone.

Pharmacological uses:

Levodopa is a precursor for dopamine and is actively transported across the intestinal wall and the blood-brain barrier by a branched chain amino acid carrier. It is an effective remedy for the relief of Parkinson's disease [10].

Beta-Sitosterol-

Structure:



IUPAC name: 17-(5-Ethyl-6-methyl heptan-2-yl) -10,13-dimethyl-1,2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[*a*]phenanthren-3-ol

Molecular formula:  $C_{29}H_{50}O$

Molecular weight: 414

Appearance: White solid

Solubility: Easily soluble in ethanol and chloroform, partially soluble in water

Pharmacological uses

Beta-Sitosterol administered alone and in combination with similar phytosterols shows immune modulatory, anti-inflammatory [21] activities.

Beta-Sitosterol shows hepatoprotective [22], antioxidant and antipyretic [23-24], rheumatoid arthritis [25], colon cancer [26], benign prostatic hypertrophy [27-28], and breast cancer [29].

### Phyto-Constituents from Medicinal Plants

Many plants contain Levodopa and betasitosterol examples are Bakala, halunda, apata, abai, kanchan, vilayati babul. We selected *Bauhinia racemosa*, *Canavalia Gladiata* and *Vigna vexillata* for analysis of Levodopa and beta-sitosterol. *Bauhinia racemosa* is well known plant in India because leaves use in festival of dasara as gold plant leaves. *Canavalia gladiata* is used in daily food in village. *Vigna Vexillata* is rare plant which is used in some ayurvedic medicine.

*Bauhinia racemosa* Lam. plant is from Caesalpiniaceae family. Common name in Marathi is apta and sona, in hindi kathamuli, in bangali banraj, in kannada vanasamtiige, in English bidi leaf tree and mountain ebony, in Sanskrit yamalpatrak. It is easily available in south Asia. Flowering season of plant is April to May and fruits season is June to august. Kumar R. *et al.* reported antioxidant and antimicrobial activities of *Bauhinia racemosa* [33]. In vitro antimicrobial activity reported by Gaurav Kumar *et al.* [34]. Borikar *et al.* Reported antiulcer activity of *Bauhinia racemosa* in rats [35]. Leaves of plants contain antihistaminic effect is proved by Nirmal *et al* [36]. Amoo *et al.* analysed seeds for extraction and physio-chemical properties of oils from seeds [37]. Darne priti reports uses and novelty of *Bauhinia racemosa* seeds oil [38]. *Bauhinia racemosa* have phenol, flavonoids, saponins, glycosides, alkaloids and tannis is reported by sharanabasappa *et al.* [39].

*Canavalia gladiata* (Jacq.) DC. is from Fabaceae family. Common name in Marathi is abai, in Malayalam valavara, in Hindi lalkududumpal, in English sword bean and broad bean. It is cultivated throughout India. Flowering season is April to October and fruits season is November onwards. *Canavalia gladiata* contain amino acid, lectins and many useful markers [40]. Lectins are presents in *Canavalia gladiata* and this lectin is useful for cgenitaxonomy [41-42]. Ekanayake S. *et al.* reports that many minerals and amino acids are presents in *Canavalia gladiata* seeds [43].

*Vigna Vexillata* L. is a plant from Fabaceae family. Common name in Marathi is halunda, in Hindi jungali mung and suryaparni, in Malayalam Kattupayar, in Sanskrit mdgaparni and in English zombie pea, wild mung and wild cow pea. Flowering season of plant is August to March. It is available in south asian counties. Leu Y.L. *et al.* shows that *Vigna vexillata* have anti-inflammatory activity and many phyto- constituent [44]. Lattanzio *et al.* reported that flavonoids are presents in vigna species plants [45]. Battu *et al.* reported that plant contain Levodopa which is useful for Parkinson diseases [46]. Adetula *et al.* shows centromeric banding pattern of mitotic chromosomes in *Vigna vexillata* (TVnu 73) [47]. Images 3, 4 and 5 represents plant *Bauhinia racemosa*, *Canavalia gladiata* and *Vigna vexillata* respectively.

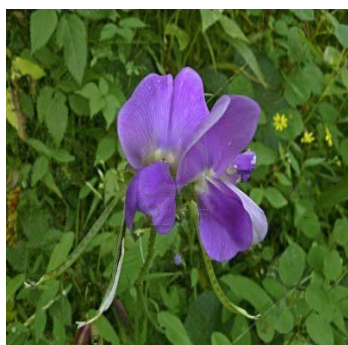




**Image 3:** *Bauhinia racemosa*



**Image 4:** *Canavalia Gladiata*



**Image 5:** *Vigna vexillata*

### Heavy Metals in Plants

Heavy metals have been defined differently by many authors depending on the angle from which each author looks at it, but toxicity, density as well as molecular weight are salient points that inevitably appear in all the definitions of heavy metals [48-49]. Heavy metals have harmful effects on living beings if it has taken in higher amounts. Heavy metal toxicity has led to various serious diseases and also extensive mortality. The human body requires a number of trace elements like Ca, Mg, Al etc. in order to maintain good health. These trace elements, essential for human nutrition are accumulated in different parts of plants transferred from the environmental conditions during their normal growth pattern [50-51]. In human beings, these elements are mostly required in amounts less than 100 milligrams per day and are present in specific tissues and fluids of body. They maintain the certain physio-chemical processes, structural components of tissues and as constituents of enzymes in many metabolic pathways [52].

On the other side, several scientific report have indicated that herbal medicines also contain the toxic heavy metals which can cause various toxic effects like cancer, liver dysfunction, lung disease, cerebral haemorrhage, alopecia etc. One of the major reasons of incorporation of toxic metals in medicinal plants is due to the increase in contamination of the general environment [53].

The roots or leaves of the plant can absorb heavy metals from the atmosphere, water and soil such as Pb, Cd, Hg and As and these can finally accumulate in the plant through the cytosol [54]. The sources of this environmental pollution are quite varied, ranging from industrial and traffic emissions to the use of purification mud and agricultural expedients, such as cadmium containing dung, organic mercury fungicides, and the insecticide lead arsenate [55]. According to the WHO (World Health Organization, 1991), lead, cadmium, chromium, and other heavy metals must definitely be controlled in medicines in order to assure their safety [56].

Herbs could turn out to be toxic if they are found to be in excess or above the permissible limits along with other impurities. So it is necessary to determine these elements accurately in trace level. Many procedures have been described in the literature for the determination of these heavy metals (Gracia *et al.*, 2000; Adeloju and Bond, 1985; Weis *et al.*, 1999) [65, 66, 67]. Atomic absorption spectroscopy is the most common analytical method for estimating the heavy metals in herbs (Sun *et al.*, 2002) [68]. In the present study we used. Atomic absorption spectroscopy used for the determination of mercury, lead, cadmium and arsenic etc. Therefore, it was imperative to screen the present state of herbal plant materials in Indian market in terms of heavy metals (Pb, Cd, As, Hg) and trace elements (Ca, Mg, Zn, Cu and Al).

### Conclusion

From this review article we conclude that medicinal plants have many properties and they played major role against various diseases. Various herbal plants and plants extracts have significant antiulcer, antipyretic, anti-diabetic and anti-cancerous activity. Our review result shows that above-mentioned medicinal plants could prevent from fever, ulcer, diabetes, and Cancer with the principle on dose-dependence. A variety of botanical products have been reported to possess that activity. Hence the review study is concluded that the herbal drug possesses antiulcer, antipyretic and to treat anti-diabetic, anti-cancerous activity and it has been proved by different animal models which give many links to develop the future trials.

Levodopa is a precursor for dopamine and is actively transported across the intestinal wall and the blood-brain barrier by a branched chain amino acid carrier. Levodopa is useful in parkinson diseases and many plants contain levodopa. It is majorly available in mucuna species. Beta-Sitosterol administered alone and in combination with similar phytoosterols shows immune modulatory, antiinflammatory activities. Beta-sitosterol is useful in many diseases. It is used as a hepatoprotective, antioxidant and antipyretic and to treat inflammatory disorders, rheumatoid arthritis, colon cancer, benign prostatic hypertrophy and breast cancer. Both of these phyto constituents are majorly available in plants. *Bauhinia racemosa*, *Canavalia gladiata* and *Vigna vexillata* contains many phyto-constituents. Phytochemical analysis of these three plants is necessary and there are rare research papers available on this three plants. These three plants are future scope for research students for quantification of phyto-constituents using different analytical techniques.

Plants contain heavy metals which are useful for human body but excess of heavy metals is toxic for human body. Herbal plant materials in India contain heavy metals (Pb, Cd, As, Hg) and trace elements (Ca, Mg, Zn, Cu and Al). Analysis of heavy metals using Atomic Absorption Spectroscopy is suitable methods for heavy metals analysis in plants.

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