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# A REVIEW ON ANTIDIABETIC AND ANTIOXIDANT ACTIVITY OF BHUNIMBADI CHURNA.

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**Abstract:** The role of natural products as a source of remedies has been recognized since ancient times. In addition the overuse of synthetic drug which result in higher incidence of adverse drug reaction, has enthused the human to revert to nature for safer herbal medicines. The current review focus on Bhunimbadi Churna Herbal formulation and its potential in the treatment of diabetes mellitus, Diabetes is world's largest endocrine disease involving metabolic disorders of carbohydrate, fat and protein and it affects nearly 1-3% of world population. The review describes various aspect of Bhunimbadi Churna like active phytoconstituents having hypoglycaemic action, pharmacological properties and mechanism of action of its ingredients. This review also focuses on the traditional therapeutic action of the Bhunimbadi Churna mention in Brhat Nighantu Ratnakar. In various pharmacological studies, done in few decades on the drugs of Bhunimbadi Churna, it has been proved that almost all the constituents of Bhunimbadi Churna, posse anti hyperglycaemic, hypolipidemic, antioxidant and other therapeutic properties.

**Keywords:** Antidiabetic, hypolipidemic, antioxidant property, Herbal

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## INTRODUCTION

Diabetes mellitus is a major public health problem. According to WHO reports, more than 176 million patients suffer worldwide and it is estimated that in 2025, there will be about 300 million patients living with this condition. The increase is expected to be 42% in developed countries and 70% in developing countries. Although different types of hypoglycaemic agents such as thiazolidinediones, insulin, biguanides and sulphunylurea are available; there is growing interest in herbal remedies due to the side effects associated with these therapeutic agents beside their limitations in managing the disease effectively.[1, 2]

Diabetes mellitus is a metabolic disorder affecting carbohydrate, fat and protein metabolism and represents a heterogeneous group of disorders characterized by hyperglycemia, which may be due to impaired carbohydrate utilization resulting from a defective or deficient insulin secretion response. Diabetes mellitus is marked by sustained hyperglycemia and has deleterious effect on kidney. The characteristic symptoms of diabetes are polyuria, polydypsia, polyphagia and unexpected weight loss[3]. *Momordica charantia, Trigonella foenumgraelum, Enicostema littorae, Gymnema sylvestre, Azadirachta indica, Syzigium cumini, Zingiber officinale, Swertia chirayata*, are some of the most effective and the most commonly studied Indian plants in relation to diabetes.

### Bhunimbadi Churna:

Bhunimbadi Churna is a group of nine drugs, which has been mentioned in Bhunimbadi Churna under Brhat Nighantu Ratnakar**.**[4] The botanical name, family and therapeutic uses of Bhunimbadi Churna as mention in Ayurvedic literature are described in Table 1.

**Table 1: Composition of Bhunimbadi Churna**

| Sr No. | Sanstrit Name | Botanical Name | Family | Therapeutic uses as described in Ayurveda[4] |
|---|---|---|---|---|
| 1 | Chirayata (Bhunimba) | *Swertia chirata* | Gentianaceae | Fever, Jaundice, Anemia, Antidiabetic |
| 2 | Indrajav | *Holarrhena antidysenterica* | Apocynaceae | |
| 3 | Sunthi | *Zingiber officinale* | Zingiberaceae. | |
| 4 | Marica | *Piper nigrum* | Piperaceae | |
| 5 | Pippali | *Piper longum* | Piperaceae | |
| 6 | Nagarmoth | *Cyperus rotundus* | Cyperaceae | |
| 7 | Katuki | *Picrorrhiza kurroa* | Scrophulariaceae | |
| 8 | Chitrak | *Plumbago zeylanica* | Plumbaginaceae | |
| 9. | Kada chhal | *Holarrhena antidysenterica* | Apocynaceae | |

**Pharmacological studies done on the drugs of Bhunimbadi Churna:**

To establish the traditional therapeutic effects on modern scientific parameters, various pharmacological studies have been done in last few decades on the drugs of Bhunimbadi Churna. Among these scientific researches only antidiabetic studies conducted on individual drugs of Bhunimbadi Churna are reviewed here. The Body weight, Blood glucose, Serum cholesterol, Serum triglyceride, Serum creatinine, Serum ALPH, Serum ALT, Serum AST, Serum bilirubin, Serum total protein, Serum albumin were observed to be elevated in diabetic patients. It is also observed that oxidative stress is one of the main contributory factors in the patho-physiology of many diseases, including type-2 diabetes mellitus. So hypolipidemic and antioxidant studies done on these drugs are also discussed here.

***Swertia chirata Buch.Ham:***

*Swertia chirata* belongs to the family Gentianaceae. The plant is a robust annual herb which grows upto 1.5 meters in height in the Himalayas[5], usually at an altitude of 4,000-10,000 feet but it can also be grown in sub-temperate regions, as well as in a variety of soil conditions.[6, 7] The compounds isolated from Swertiachirata include a large number of xanthones, glycosides, alkaloids and other compounds like chiratin, ophelic acid, palmitic acid, oleic acid, stearic acid. The first isolated dimeric xanthone was chiratanin. Other important phytoconstituents include swerchirin, swertiamarin, swertanone, mangiferin, amarogentin, gentiopicrin and chiratol.[8, 9] Chiretta stimulates the digestion and helps to normalize blood sugar, which makes it useful for diabetics. Studies with animals suggest that this herb reduces the sugar levels only when they are high, which lowers the risk of hypoglycemia.[10] Also 95% ethanol extract and four fractions of *Swertia chirayita* were tested for blood sugar lowering activity in rats. The hexane fraction caused maximum lowering although the ethanol extract was clearly active.[11] Swertiamarin is main constituents of plant given the anti-diabetic effect due to an active metabolite, gentianine, that upregulates PPAR-γ gene expression in 3T3-L1 cells.[12] A xanthone compound, mangiferin effect on the atherogenic potential of streptozotocin (STZ)-diabetes was investigated.[13, 14] S*wertia chirayita* possesses *in vitro* and *in vivo* antioxidant activity, the liver and kidney of $CCl_4$-intoxicated animals exhibited decrease in superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) levels. Additionally, these organs exhibited increase in malondialdehyde (MDA) level.[15] Out of seven compounds extracted from this plant, five components exhibited antioxidant activity at different magnitude of potency.[16] Figure 1 *Swertia chirata* whole plant.

***Holarrhena antidysenterica Wall:***

Drug consists of dried seeds of *Holarrhena antidysenterica* Wall belonging to family Apocynaceae. In Sanskrit called Bhadra Yava and in Hindi Indraju. The seeds were also reported

to possess steroidal type alkaloids. Seeds are very useful in case of colitis and bleeding problems, diarrhoea and dysentery.[17] It also uesd as antioxidant, antihyperglycemic, anti-malarial, spasmolytic and spasmogenic properties.[18] The hypoglycemic effect of ethanolic extract of its seeds in streptozotocin – induced diabetic rats and its effect on serum cholesterol, triglyceride, aspartate transaminase (AST), alanine transaminase (ALT), alkaline transferase (ALP), total protein, urea, creatinine and uric acid and indicated of its potent antidiabetic effect.[19] Also studied the present experiment was conducted to search out the effect of hydro-methanolic extract of seed of *Holarrhena antidysenterica* on intestinal α-glucosidase activity in dose dependent manner and on the management of postprandial hyperglycemia in starch loaded rats.[20] The *Holarrhena antidysenterica* seeds crude methanolic extract and ethyl acetate fraction indicated significant antioxidant activities in doze dependant manner and revealed maximum scavenging activity 68% and 80% at concentration of 250µg/mL.[21] Figure 2 *Holarrhena antidysenterica* seed.

***Zingiber officinale* Roxb:**

The rhizome of *Zingiber officinale*, is one of the most widely used species of the ginger family (Zingiberaceae) and is a common condiment for various foods and beverages. Ginger has a long history of medicinal use dating back 2,500 years in China and India for conditions such as headaches, nausea, rheumatism, and colds.[22] Ginger is a rich source of volatile oil. Zingiberene, zingiberol, β-sesquiphellandrene, β-bisabolene, α-farnesene, ar-curcumene and smaller amounts of camphene, β-phellandrene, cineole, geraniol, curcumene, citral, terpineol, borneol important constituents of the plant.[23] A methanolic extract of dried rhizomes of ginger produced a significant reduction in fructose-induced elevation of lipid levels, be achieved with a dietary supplement of either ginger or its extract containing aldose reductase inhibitors.[24] Antidiabetic potential of *Zingiber officinale* was mainly through inhibition of the glucose diffusion and to a limited extent by reducing the glycation.[25] The antioxidant properties of [6]-gingerol which is very effective agent for anticipation of ultra violet B (UVB)-induced reactive oxygen species production and COX-2 idiom, and a promising therapeutic agent against UVB induced skin disorders, has been studied both *in-vitro* & *in-vivo*. It also has a protective role to toxicity and lethality against some agent like carbon-tetra chloride, cisplatin etc.[26] Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant.[27] The effect of (S)-[6]-gingerol increased glucose uptake in L6 skeletal muscle cells by activating AMPK. (S)-[6]-gingerol, a major component of *Zingiber officinale*, may have potential for development as an antidiabetic agent.[28] Anti-hyperglycaemic, lipid lowering and anti-oxidant properties of [6]-gingerolin db/db mice.[29] Figure 3 *Zingiber officinale* rhizome.

***Piper nigrum* Linn:**

*Piper Nigrum* Linn (Black pepper) is a viny perennial plant producing berry-like and aromatic pungent fruits. It is locally known as "pamienta" or "paminta" Which belongs to family Piperaceae. Although black pepper is cultivated in many tropical regions, it is native to Kerala State in India where it still occurs wild in the mountains.[30] Piperine the major active principle of black pepper, is closely related in structure to the known natural carcinogens-safrole, estragole and methylengenol which are also widely distributed in spices and plant oils. The plants contains mainly alkaloids, amides, propenyphenols, lignans, neolignans, terpenes, steroid, piperolides, chalcones, dihydrochalcones, brachyamide, piperamide, piperamine, piperettine, pipericide, piperine, piperolein, trichostachine, sarmentine, sarmentosine, tricholein, retrofractamide.[31] The effect of piperine on blood glucose level in alloxan-induced diabetic mice in acute and subacute study models.[32] Oxidative stress plays a key role in diabetes, and treatment with *P. nigrum* and *V. rosea* are useful in controlling not only the glucose and lipid levels but these components may also be helpful in strengthening the antioxidants potential.[33] The subacute administration of piperine has statistically significant antihyperglycemic activity while acutely it raises blood glucose at high doses.[34] Figure 4 *piper nigrum* fruits.

***Piper longum* Linn:**

*Piper longum* L. (Piperaceae), commonly known as "long pepper", is widely distributed in the tropical and subtropical regions of the world.[35] Piperine is the major and active constituent of long pepper. The fruits gave positive tests for the presence of volatile oil, starch, protein and alkaloids, saponins, carbohydrates, and amygdalin and negative test for tannins.[36] The antihyperglycemic and antilipidperoxidative effects of ethanolic extract of *Piper longum* dried fruits in alloxan-induced diabetic rats were studied.[37] The blood glucose level, carbohydrate metabolizing enzymes and the status of lipid peroxidation and antioxidants were assayed using specific colorimetric methods. Oral administration of dried fruits has shown significant anti-hyperglycemic, antilipidperoxidative and antioxidant effects in diabetic rats comparable to that of the standard reference drug glibenclamide.[38] The antidiabetic and antihyperlipidemic potential of oil from *Piper longum* and piperine was investigated with their possible mechanism using α-glucosidase, aldose reductase (AR), and pancreatic lipase inhibitory activity.[39] Figure 5 *piper longum* fruits.

***Cyperus rotundus* Linn:**

*Cyperus rotundus* Linn belong to the family Cyperaceae, also known as purple nutsedge or nutgrass, is a common perennial weed with slender, scaly creeping rhizomes, bulbous at the base and arising singly from the tubers which are about 1-3 cm long. The tubers are externally blackish in colour and reddish white inside, with a characteristic odour. Different phytochemical

studies on *C.rotundus* revealed the presence of alkaloids, flavonoids, tannins, starch, glycosides, furochromones, monoterpenes, sesquiterpenes, sitosterol, fatty oil containing a neutral waxy substance, glycerol, linolenic, myristic and stearic acids.[40] Oral daily administration of 500 mg/Kg of the extract (Once a day for seven consecutive days) significantly lowered the blood glucose levels in rats with alloxan induced diabetes.[41] The scientists concluded that this antihyperglycemic activity can be attributed to its antioxidant activity as *C.rotundus* showed a strong 1,1-diphenyl-2-picryihydrazyl (DPPH) radical scavenging action *in-Vitro*. These results are convergent with *C.rotundus* potential to suppresses AGE formation and protein oxidation in a model of fructose-mediated protein glycoxidation.[42] Amrita Bindu, a salt-spice-herbal mixture containing *C. rotundus* Linn exerts a promising antioxidant potential against the free radical 2, 2'-azinobis (3-ethylbenzoline-6 sulphonacid).[43] Figure 6 *cyperus royundus* rhizome.

***Picrorhiza kurroa* Royle ex Benth:**

*Picrorhiza kurroa* is a small perennial herb from the Scrophulariaceae family, found in the Himalayan region growing at elevations of 3,000-5,000 meters. *Picrorhiza kurroa* has a long, creeping rootstock that is bitter in taste, and grows in rock crevices and moist, sandy soil. Kutkin is the active principal of *Picrorhiza kurroa* and is comprised of kutkoside and the iridoid glycoside picrosides I, II, and III.[44, 45] *P. kurroa* extracts are able to ameliorate biochemical damages induced by alloxan in diabetic rats.[46] Also the standardized extract of Picrorhiza kurroa possess significant antidiabetic activity in streptozotocin-nicotinamide induced type-2 diabetes mellitus in rats.[47] All the extracts of *picrorhiza kurroa* and isolated compounds were evaluated for its antioxidant activity using two assays, 2,2-diphenyl-1-picrylhydrazyl radical and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) assay.[48] The ethanol extract of rhizome of *Picrorhiza kurroa* , at the dose of 20mg/kg body weight , accelerated the healing of stomach wall of indomethacin induced gastric ulcerated rats by an *in vivo* free radical scavenging action.[49] The anti-oxidant effect and the therapeutic dose and time window of picroside II by orthogonal test in cerebral ischemic injury in rats. The forebrain ischemia models were established by bilateral common carotid artery occlusion (BCCAO) methods.[50] The oral administration of aqueous and methanol extracts of *P. kurroa* rhizomes (250 and 500 mg / kg body weight / day) for 15 days significantly reduced blood glucose, glycosylated haemoglobin and increased total hemoglobin, plasma insulin in alloxan-induced diabetes in albino rats. The treatment also showed significant correction in the level of nitric oxide radicals, superoxide radicals, peroxynitrite radical, lipid peroxidation, glutathione, glutathione reductase, glutathione-S-transferase, glutathione peroxidase, superoxide dismutase and catalase in the pancreas of alloxan diabetic rats.[51] Also study shows that picroliv, picroside-I and kutkoside possess the properties of antioxidants which appear to be mediated through activity like that of

Superoxide dismutase, metal ion chelators and xanthine oxidase inhibitors.[52] Figure 7 *Picrorhiza kurroa* rhizome.

***Plumbago zeylanica* Linn:**

Chitrak consists of dried mature root of *Plumbago zeylanica* Linn. Belong to family Plumbaginaceae, a large perennial subs-candent shrub, found throughout India in wild state and occasionally cultivated in gardens.[53] Naphthaquinones, alkaloids, glycosides, steroids, triterpenoids, tannins, phenolic compounds, flavanoids, saponins, coumarins, carbohydrates, fixed oil and fats and proteins of all the chemical constituents plumbagin is the principle active compound.[54] Pharmacological studies carried out have indicated that *P.Zeylanica* has antihyperglycemic effect on diabetic induced animals. The ethanol extract of *P.Zeylanica* root on key enzymes of glycolysis and muscle hexokinase, phosphofructokinase, pyruvate kinase lactate dehydrogenase activities were diminished in diabetic rats.[55] Also the evaluate the antidiabetic effects of plumbagin isolated from *P. zeylanica* L. root and its effect on GLUT4 translocation in STZ-induced diabetic rats.[56] Also shows that oral administration of ethanolic root extract of *P. Zeylanica* (100 mg, 200 mg/kg/p.o), tolbutamide (250 mg/kg/p.o) increased the activity of hexokinase and decreased the activity of glucose-6-phosphatase ($P < 0.001$) in streptozotocin treated diabetic rats.[57] *In-vitro* antioxidant and Total Phenolic Content (TPC) assay conducted on methanolic extract of the roots indicated *P. Zeynalica* to be a potent radical scavenger. The inhibition percentage by DPPH method was seen to be 88.45 % compared to ascorbic acid (96.5 %).[58] *P. Indica* roots are indeed rich in phytochemicals and had substantial antioxidant activities, implying that *P. Indica* roots can be used as a potential source of natural antioxidant.[59] The isolation and spectral data for new flavonoid 2-(2,4-Dihydroxy-phenyl)-3,6,8 trihydroxy chromen-4-one from the roots of *P. Zeylanica* were determined the antioxidant activity was studied by free radical scavenging and superoxide radical scavenging methods.[60] Figure 8 *Plumbago zeylanica* root.

***Holarrhena antidysenterica* (Roth) A. DC:**

*Holarrhena antidysenterica (Linn.)* Wall is a genus of trees or shrubs found in the tropics and subtropics of the old world. It comprises seven or eight species, which are distributed in Asia, tropical areas of Africa, Madagascar, India, Philippines and Malayan Peninsula. The plant is well known as 'Kurchi'. The bark is thick, brown and rough, with abundant milky white latex. The bark and seeds are bitter, constipating, astringent, acrid, refrigerant, anthelmintic, antiperiodic, aphrodisiac, carminative, expectorant, frebrifuge and tonic. They are useful in amoebic dysentery, diarrhoea, asthma, hepatopathy.[61] *Holarrhena antidysenterica* is also a rich source of other steroidal alkaloids such as kurchine, kurchimine, conessidine, holarrimine, conessidine, conkurchicine and regholarrhimine.[62] Bark powder of *H.antidysenterica* was subjected to hot

continuous extraction (soxhlet) with various solvents like Alcohol, butanol, chloroform, aqueous and butanone showed significant antidiabetic activity in acute as well as prolonged treatment compared to control.[63] Methanolic extract of bark possesses antihyperglycemic activity with antihyperlipidemic and antioxidant potential which may prove beneficial in cardiovascular complications associated with diabetes mellitus.[64] *Holarrhena antidysenterica* also show in-vitro antioxidant potential according to FTC assay method.[65] *Holarrhena antidysenterica* bark has both antihyperglycemic and antioxidant potential but no acute toxic effect.[66] Figure 9 *Holarrhena antidysenterica stem bark.*

**CONCLUSION:**

Diabetes mellitus is a metabolic disorder caused due to relative or absolute deficiency of insulin or insulin resistance at the cellular level. This review article has presented the Antidiabetic action of Bhunimbadi Churna, a group of nine plants which has been mentioned in Brhat Nighantu Ratnakar. It showed that these plants have varying degree of hypoglycemic activity along with antioxidant property. The Antidiabetic activity of these plants are attributed to the presence of polyphenols, terpenoids, alkaloids, flavonoids, glycosides and other active constituents, which shows reduction in blood glucose level. Numerous mechanisms of action have been predicted for these plant extracts. Some herbal drugs have effects on the activity of pancreatic β-cells (insulin release, β-cell regeneration) or some drugs enhance the insulin sensitivity and some of the plant extracts exhibit insulin-like activity. Other mechanism may involve improved glucose homeostasis (increase of peripheral utilization of glucose, increase or decrease of glycogenolysis), inhibition of intestinal glucose absorption, reduction of glycemic index of carbohydrates, reduction the effect of glutathione. All the actions may be responsible for the reduction and abolition of diabetic complications. Thus there is need for more investigation to evaluate the mechanism of action of these medicinal plants of Antidiabetic effect. Future it required for the Antidiabetic effect of these drug in clinical setting with appropriate parameters.

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**Figure 1**

**(*Swertia chirata*Whole plant)**

**Figure 2**

**(*Holarrhena antidysenterica* seed)**

**Figure 3**

**(*Zingiber officinale* Rhizome)**

**Figure 4**

**(*Piper nigrum* Fruit)**

**Figure 5**

**(*Piper longum* Fruit)**

**Figures 6**

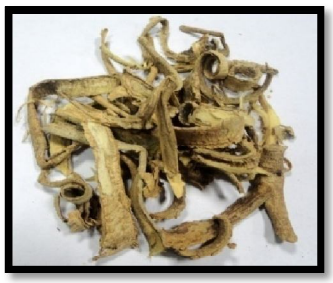
**(*Cyperus rotundus* Linn Rh)**

**Figure 7**

**(*Picrorrhiza kurroa* Rh)**

**Figure 8**

**(*Plumbago zeylanic* Root)**



**Figures 9**

**(*Holarrhena antidysenterica* St Bk.)**

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