International Journal of Advanced Technology in Engineering and Science
Vol. No.4, Issue No. 06, June 2016
www.ijates.com
ijates
ISSN 2348 - 7550

ANTI-DIABETIC AND OTHER PHARMACOLOGICAL ACTIVITIES OF CASSIA FISTULA

Tanushri Joshi[1], Muskan Agarwal[2], Tanya Singh[3]
Shahrukh Husain[4], Trisha Pruthi[5], Rachana[6]

[1,2,3,4,5,6]*Department of Biotechnology,*
JayPee Institute of Information Technology, Noida, (India)

ABSTRACT

In Indian system of medicine,Ayurveda is practiced since a long time in order to lead a disease free life. It is one of the few countries where almost all the known medicinal plants can be cultivated in some part of the country or the other and it is taking the world towards prevention rather than cure through the help of herbal medicinal plant. Cassia fistula is one such plant that is used to cure various ailments. This medicinal plant finds application in pharmaceutical, cosmetic, agricultural and food industry. C. fistula iscarries many properties like:antioxidant, wound healing, hepatoprotective, anti-diabetic and many other activities.There are several in vitro and in vivo studies performed provingthe hyypoglycemic effects of different parts of this plant. Now scientists are trying to enhance these effects by combining the traditional knowledge with the latest technology: nanotechnology. The present review describes and discuses important studies carried out for proving the anti diabetic effects of Cassia fistula.

Keywords*: *Antioxidantactivity,Cassia fistula, Diabetes mellitus,Gold and silver nanoparticles, Hepatoprotective, Wound healing.

I. INTRODUCTION

Medicinal plants in India are considered as a vast and important source of several pharmacologically principles and compounds that can be used as home remedies against multiple ailments.[1] Ayurveda is practiced here since a ancient time, in order to lead a disease free life.[2] Natural therapy always believe more in prevention rather than curing a disease with the help of natural products obtained from natural resources like plants and herbs etcAmong such plants one such example is ***Cassia fistula,*** which is an IndianLabernumis also popularly known as the**golden shower tree**in India**.**It is anangiosperm, which belong to the family Fabaceae.This species is an important part of Indian subcontinent, Southeast Asia and Sri Lanka.[3] This beautiful tree is also known as Amaltas, is usually medium in size and has dark green compound leaves that are large in size.[1, 4] The flowers of *Cassia fistula* are bright yellow in colour, with hard, durable and heavy wood (Figure 1).[4] It is extensively used for making cabinets,templedrums, inlays work, fence posts, and agricultural implements and also in construction of houses, bridges etc. Studies prove that *Cassiafistula* has remarkable antioxidant, wound healing, hepatoprotective and anti-diabetic activity etc.[1, 2, 4,]

Figure 1 Cassia fistula

Diabetes is a widespread systemic disease affecting a major proportion of the worldwide population. It is a group of metabolic diseases where the blood glucose level of a persongoes high as, either the insulin production in his body is insufficient or,glucose utilizing cells don't respond to insulin, or both.[5]Currently available therapeutic options for diabetes are: insulin shots and oral hypoglycemics which are not always successful and satisfactory in maintaining normal blood glucose level. Moreover, the complications associated with the regular treatment of this chronic disease increase the need for an alternative that is effective, inexpensive, safer, as well as affordable to the patient. Scientific studies of the glucose lowering/hypoglycemic effect of the aqueous and methanol extracts of all the parts of *Cassia fistula* in both normoglycemic as well as, Type 2 diabetic rat's (STZ induced)reveals about its anti-diabetic properties.[6] Researchers are now exploring nanotechnology for treating various diseases, including diabetes mellitus.There are studies based on Gold and silver nanoparticles whichreport that *Cassia fistula* have remarkable anti-diabetic properties. Gold nanoparticles are synthesised using the aqueous extract from stem bark of *Cassia fistula* analysing itshypoglycaemic effects.

II. PHYTOCHEMICAL COMPONENTS OF CASSIA FISTULA

There are various primary and secondary metabolites of *Cassia fistula*which are thought to be responsible for its biological effects. These components are analysed in seed, stem, pollen, fruit and pod of this plant.This plant is known as a rich source of tannins, flavanoids, anthroquinone, amino acids, phenols, lipids and glycosides and is medicinally important and nutritionally valuable.[1]Different parts of *C. fistula* are highly rich in phytochemicals. Root bark of this plant contains an important chemical called fistucacidin (a hydroxyl anthraquinone type compound), tannin, and oxyanthroquinone and phlobaphenes substances.[7]Leaves contain volatile oils,rhenin glycosides, Sennoside-A and Sennoside –B, tannins, and kaempferol glycosides.[8]Fistulic acid is obtained from pods. Compounds like sitosterol, leucopelargonidin, kaempferol, fistulin, new bianthraquinone, glycosides, Ceryl alcohol and a mixture of flavonoids and glucosides are present in flowers.[9]Pulp contains gum, sugar, gluten, anthraquinone glycosides, rhein, sennosides A and B, water and coloring matter.[10]Given below, Table 1 shows the primary and secondary components of various parts of *Cassia fistula* and their traditional uses.[9, 11, 12]

Table 1.Primary and Secondary metabolites in *C. fistula*,plant parts along with their traditional uses.

Parts of *Cassia fistula*	**Primary metabolites**	**Secondary metabolites**	**Traditional uses**
Seed	free amino acids, galactomannan free sugars	17-norpimar-8(9)-en-15-one Chrysophanol	Skin diseases, fever, abdominal pain, constipation
Flower	Lipids, proteins, DNA, phenols, soluble sugar, starch	Kaempferol, rhein, fistulin, alkaloids, leucopelargonidin tetramer triterpenes, ceryl alcohol	For stomach troubles, leprosy, fever, abdominal pain
Root	Proteins, lipids, sugar, starch	Rhamnetin-3-O-gentiobioside,	Used against cardiac disorder, skin diseases, ulcer
Pulp	Sugar, starch, formic acid, butyric acid , oxalic acid	Volatile oil, Rhein, gum, gluten, sennosides A and B	Liver disorder, in biliousness, and also used as a tonic And can be applied in gout, rheumatism, diabetes, against malaria and black water fever, diabetes,
Leaves	Chlorophyll a and b, caretenoids, starch, lipids	biflavonoids, triflavonoids, rhein, rheinglucoside, sennoside A and B	Laxative properties
Pod	5-nonatetracontanone, 2-hentriacontanone, triacontane, 16-hentriacontanol and sitosterol along with an oil	3-formyl-1-hydroxy-8-methoxyanthaquinone, Fistulic acid	Used as laxative drugs in traditional medicines

III. PHARMACOLOGICAL STUDIES OF CASSIA FISTULA: THE DISEASE KILLER

In Ayurveda, the golden shower tree is known as *aragvadha*, which means- "disease killer"[13].Various parts of the tree like: bark, root, flowers, leaves, fruit pulp are used in the field of medicine and have many health benefits.[1,2] The tree has anti diabetic, anti-tumour, hepato protective, antifertility,cholesterol lowering, astringent, febrifugal, and purgative, anti inflammatory, antibacterial, antioxidant, antiviral, anti dysenteric properties etc.[2,12,13] It also alleviates symptoms and pain of arthritis, gout, nervous system diseases, eczema, ringworm, leucoderma, leprosy etc.[2]Given below are some therapeutic uses of *Cassia fistula*.

3.1 Antioxidant activity

Antioxidants are natural or manmade substances which may prevent or delay cell damage by scavenging free radicals and other oxidants. These free radicals lead to the formation of chain reactions that may damage cells as they tend to oxidize biomolecules like, cellular proteins, lipids genetic materials etc altering their structures and functions.[17] Antioxidants like thiols or ascorbic acid (vitamin C), phenols etc can terminate these chain reactions.Phenolic compounds are the secondary metabolites obtained from natural sources which have great antioxidant potential.They can easily breakdown the chain reaction by radical scavenging. It was shown by Irshad, Md, et al. (2012) that methanolic extract of pulp and seed showed the lowest EC_{50}, 0.915 and 1.088 mg/mL for DPPH scavenging activity. They have also performed various other antioxidant measurements for this plant and found *C. fistula* to a very good radical scavenger. The antioxidant potential of this plant could be directly linked to its phenolic content. [28.] Various other antioxidant studies performed by many other scientists are tabulated in table 2 as below.

Table2. Different studies on antioxidant activity of *Cassia fistula.*

Part of plant	**Type of extract**	**Portion of the plant containing antioxidant activity (relative)**	**References**
Seed and pulp	Methanolic and Hexane extract	MEP>MES>HEP>HES	Irshad et al (2012)
Flower	Hydroaclcoholic extract	Flower	Bhalodia et al (2011)
Leaves, Flowers, Stem and pod	Methanolicextraxt	Flower>Pod>>stem>leaf	Nehru et al(2008)
Stem bark, fruit pulp, flower and leaf	Methanolic and ethanolic extract of leaf only.	Stem bark and leaves	Sidhuraja et al (2002)

3.2 Hepatoprotective activity

Hepatotoxicity is a condition when liver is damaged, which can lead to malfunctioning to liver, or to function irregularly.One of its most important tasks is to filter out toxic substances from the body, including alcohol, carbon tetra chloride (CCl_4), different medications like paracetamol, chemotherapyand antibiotics etc. Dawada et al.(2012)observed that ethanolic extract of *Cassia fistula's* root can be protective against CCl_4 induced hepatotoxicity.[14] This study was conducted by injecting CCl_4 and Olive Oil, in ratio 1:1; 2ml/kg, to adultWistar albino rat's colony. The rats were divided into 6 groups for 7 days: I-control, II-CCl_4treated, III- standard silymarine treated, IV-ethanol extract(100 mg), V- ethanol extract (200mg).The levels of the marker enzymes (SGOT, SGPT, ALP, bilirubin) of liver functions were initially elevated, and then start decreasing. There was an

increase in the body weight in rats. The Serum total protein and the Serum albumin also reached normal level. *C.fistula* (200g/kg and 100g/kg) showed comparable results with a standard drug Silymarin. In another study even ethanolic extract of leaves of *Cassia* were found to have hepatorptoective activity against Diethyl nitrosamine.[15]

3.3 Wound healing

One experimental study suggests that *Cassia fistula* can be used in healing, as well. In a study conducted on albino rat model found out that ethanolic extract of leaves of *C. fistula* could kill microbes like *Staphylococcus aureus* ATCC 29213 and *Pseudomonas aeruginosa* ATCC 27853. The ethanolic extract was applied in the form of a formulation and it was observed that formulated ointment could treat rats in terms of better wound closure, improved tissue regeneration at the wounded site.[16]

IV. ANTI-DIABETIC EFFECT OF CASSIA FISTULA

Diabetes is a disease that affects your body's ability to produce or use insulin. Food consumed by our body is converted into sugar or glucose and transported to blood and then to other sites. The level of glucose is maintained in the blood with the help of insulin and insulin target tissue/organs. There are two main types of diabetes: Type 1 and Type 2.In case of type 1 diabetes, pancreas does not produce enough insulin to maintain normal glucose level. It is also called juvenile diabetes, since it is often diagnosed in children or teens, whereas type 2 diabetes occurs when the body is unable utilize insulin often termed as insulin resistance.[19] Type 2 diabetes is commonly called "adult-onset diabetes".The cause of diabetes is unclear, but genetics, diet, obesity and lack of exercise do play a role in developing diabetes, particularly Type 2 diabetes.[5]

John Wilking Einstein et al.(2013)didcomparative evaluation of anti-diabetic effects of methanol extractsofdifferent parts of *Cassia fistula.*[20]The extract was tested innormoglycemic as well as, streptozotocin-nictotinamide induced type 2 diabetic rats. Different extracts of *Cassia fistula* were administered(for 21 days) to the diabetic rats at 250 mg/kg and 500 mg/kg doses.Biochemical parameters like insulin, blood glucose, glycosylated hemoglobin, serum marker enzymes and lipid profile were determined. The methanol extract of leaves and the bark showed to be more effective in causing hypoglycemia in normoglycemic rats. After oral administration of the bark and leaf methanolic extracts, the diabetic rats that showedthatincreased levels of glycosylated haemoglobin, plasma insulin, were reverted to near normal levels. Glucose uptake studies in isolated rat hemidiaphragm showed enhanced peripheral utilization of glucose. Dose of 500 mgkg−1 of methanol extract of the leaves and bark showed significant antilipidemic and antihyperglycemicactivity,as well. The extracts also showed improvement in parameters like insulin profile and glycosylated haemoglobin as well as, in the regeneration of pancreatic βcellsand so might be of value in treatment of diabetes. Further investigation is required to identify the exact phytoconstituent(s) of *Cassia fistula* that are responsible for its anti-diabetic effect.Daisy et al. (2010)also conducted an experiment showing insulin mimetic impact of Catechin (isolated from *Cassia fistula*) on the oxidation of glucoseand molecular mechanisms of its uptake on Streptozotocin-induced diabetic Wistar rats.[6]

V. NANOTECHNOLOGY AS A TREATMENT FOR DIABETES MELLITUS

Today Diabetes is considered to be one of the serious problems of modern western society. The disease is rapidly rising all over the world at an alarming rate. Reportedly, in view of undesirable side effects of orthodox medication and therapies, a search is on to find out ways to avoid some of these by using drugs that produce same results but have no or little side effects.[21] The latest advancement in this search is using nanotechnology, it is being used to create a smart delivery system that maintains the glucose levels from within the body effectively, by replicating the work of the pancreatic cells that produce insulin.[22]

Gold, Silver and ZnO nanoparticles have been synthesized by various scientists from the aqueous extract of *Cassia fistula* and have been proposed to play a significant role in controlling diabetes[23, 24, 25, 26]For the synthesis of nanoparticles the use of plants is considered to be low cost, rapid eco-friendly. Reports are on the biogenesis of silver nanoparticles using mixture of leaf extracts of *Cassia fistula* and AgNO3 solution in 1:9 ratios.[27]

ZnO nanoparticles are reported to have antioxidant, antimicrobial and photodigestive activities. They were synthesized using aqueous extracts of *Cassia fistula* plant, employing solution combustion method.[26]

Daisy *et al*. (2012) investigated gold nanoparticles synthesized from aqueous extract of *Cassia fistula* stem bark in adult male Albino Wistar rats (normal and streptozotocininduced diabetic).[25] Results were compared among the normal rats given aqueous extract of *Cassia fistula* (60mg/kg bw) or phytochemically synthesised gold nanoparticles, streptozotocin induced rats given aqueous extract of *Cassia fistula* stem bark or gold nanoparticles synthesized by *Cassia fistula* and the diabetic rats administered with insulin (3IU/kg) for 30 days.

It was observed that the use of gold nanoparticles reduced serum blood glucose concentrations, increased the body weight, increased activity of alanine transaminase and aspartate transaminase, achieved an improved lipid profile and reversed renal dysfunction. Impact of gold nanoparticles was better than that of the aqueous extract of *Cassia fistula* and was comparable to that of insulin. Hence, this study indicates higher probability of phytochemically synthesized gold nanoparticles, to act as hypoglycemic agents in the treatment of diabetes mellitus.

VI. CONCLUSION

Cassia fistula is a traditional medicinal plant of India and other neighbouring countries and has immense potential to be used as hepatoprotective, antioxidant, and wound healing agent. Evidences as above proves the antidiabetic potential of this plant at glucose lowering as well as insulin synthesis level. Moreover, combining this knowledge with nanotechnologyhas shown better results against diabetes mellitus. This proves that *Cassia fistula* is a very important and useful medicinal plant that needs to be investigated further in depth for the development of modern drug in order to control various diseases.

Acknowledgement

The Authors are thankful to the Jaypee Institute of Information Technology, Noida for providing us all the facilities to carry our work on time. We owe a deep sense of gratitude to Dr. Rachana, Associate Professor, Department of Biotechnology, JIIT, Noida, for her kind help and cooperation throughout our study.

REFERENCES

[1] Danish, M., Singh, P., Mishra, G., Srivastava, S., Jha, K. K., &Khosa, R. L. *Cassia fistula* Linn. (Amulthus)-An important medicinal plant: A review of its traditional uses, phytochemistryand pharmacological properties. *J Nat Prod Plant Resour*, *1*(1), 2011,101-118.

[2] Sangu, P. K., Sharma, B. K., Rajashekharan, R., Prasad, G. P., & Ala, N. Medicinal Properties of Aragvadha (*Cassia fistula* Linn.). *International Journal of Ayurvedic Medicine*, *1*(3),2011.

[3] Neelam, C., Ranjan, B., Komal, S., &Nootan, C. Review on *Cassia fistula*. *International Journal of Research in Ayurveda and Pharmacy*, *2(2)*, 2011,426-430.

[4] Bhalerao, S. A., &Kelkar, T. S. Traditional medicinal uses, phytochemical profile and pharmacological activities of *Cassia fistula* Linn.*Int Res J BiolSci*, *1*(5), 2012, 79-84.

[5] Begum, S. A., Afroz, R., Khanam, Q., Khanom, A., & Choudhury, T. S. Diabetes Mellitus and Gestational Diabetes Mellitus. *Journal of Paediatric Surgeons of Bangladesh*, *5*(1), 2015, 30-35.

[6] Daisy, P., Balasubramanian, K., Rajalakshmi, M., Eliza, J., &Selvaraj, J. Insulin mimetic impact of Catechin isolated from *Cassia fistula* on the glucose oxidation and molecular mechanisms of glucose uptake on Streptozotocin-induced diabetic Wistar rats. *Phytomedicine*, *17*(1), 2010, 28-36.

[7] Gupta, A. K. Quality standards of Indian medicinal plants. Volume1. *Quality standards of Indian medicinal plants. Volume 1*, 2003.

[8] Khare, C. P. *Indian medicinal plants: an illustrated dictionary*. Springer Science & Business Media, 2008, 128.

[9] Chopra, R. N., Nayar, S. L., & Chopra, I. C. Glossary of Indian medicinal plants, national institute of sciencecommunication and information resources. CSIR, New Delhi,2006

[10] Agarwal, S. S. *Clinically useful herbal drugs*. Ahuja Book Company Pvt. Ltd, 2005.

[11] Sharma, B. L., Singh, D., Sharma, S. K., Hashmi, A., Singh, A., & Bansal, A. Studies on some primary metabolite's extraction and quantification in different plant parts of selected cassia species. *Asian Journal of Pharmaceutical and Clinical Research*, *6*(2), 2013, 309-314.

[12] Bahorun, T., Neergheen, V. S., &Aruoma, O. I. Phytochemical constituents of *Cassia fistula*. *African journal of Biotechnology*, *4(13)*, 2005.

[13] Sridevi, V., & MVV, C. L. A Review on Subsistence and Significance of Medical Plants Available in Andhra University, Visakhapatnam.*International Journal of Engineering and Innovative Technology (IJEIT)*, *3*(2), 2013, 326-332.

[14] Dawada, S. A. G. A. R., Varsha, Z., Dabhadkar, D. I. N. E. S. H., &Shital. P. Hepatoprotective Activity of *Cassia fistula* root against Carbon tetrachloride-Induced Hepatic Injury in rats (Wistar). *International Journal of Pharma Sciences and Research (IJPSR)*, *3*, 2012, 368-378.

[15] Pradeep, K., Raj Mohan, C. V., Gobianand, K., &Karthikeyan, S. Protective effect of *Cassia fistula* Linn. ondiethylnitrosamine induced hepatocellular damage and oxidative stress in ethanol pretreated rats. *Biological research*, *43*(1), 2010, 113-125.

[16] Kumar, M. S., Sripriya, R., Raghavan, H. V., &Sehgal, P. K. Wound healing potential of *Cassia fistula* on infected albino rat model. *Journal of Surgical Research*, *131*(2), 2006, 283-289.

[17] Valko, M., Leibfritz, D., Moncol, J., Cronin, M. T., Mazur, M., &Telser, J. Free radicals and antioxidants in normal physiological functions and human disease. *The international journal of biochemistry & cell biology*,*39*(1), 2007, 44-84.

[18] Bhalodia, N. R., Nariya, P. B., Acharya, R. N., & Shukla, V. J.Evaluation of in vitro antioxidant activity of flowers of *Cassia fistula*Linn.*International Journal of PharmTech Research*, *3*(1), 2011, 589-599.

[19] Samadder, A., &Khuda-Bukhsh, A. R. Nanotechnological approaches in diabetes treatment: A new horizon. *World J Transl Med*, *3*(2), 2014, 84-95.

[20] Einstein, J. W., MohdRais, M., &Mohd, M. A. Comparative evaluation of the antidiabetic effects of different parts of *Cassia fistula* Linn, a Southeast Asian Plant. *Journal of Chemistry*,2013.

[21] Samadder,A. &Khuda-Bukhsh,A. R. "Nanotechnological approaches in diabetes treatment: A new horizon.*World journal of Translational Medicine-Baishideng publishing*, 2014.

[22] Subramani, K., Pathak, S., &Hosseinkhani, H. Recent trends in diabetes treatment using nanotechnology. *Dig J Nanomat Biostructures*,*7*(1), 2012, 85-95.

[23] Lin, L., Wang, W., Huang, J., Li, Q., Sun, D., Yang, X.,Wang, Y. Nature factory of silver nanowires: Plant-mediated synthesis using broth of *Cassia fistula* leaf. *Chemical Engineering Journal*, *162*(2), 2010, 852-858.

[24] Daisy, P., &Saipriya, K. Biochemical analysis of *Cassia fistula* aqueous extract and phytochemically synthesized gold nanoparticles as hypoglycemic treatment for diabetes mellitus. *Int J Nanomedicine*, *7*, 2012, 1189-1202.

[26] Zak, A. K., Majid, W. A., Mahmoudian, M. R., Darroudi, M., &Yousefi, R. Starch-stabilized synthesis of ZnOnanopowders at low temperature and optical properties study. *Advanced Powder Technology*, *24*(3), 2013, 618-624.

[27] Indhumathy, J., Gurupavithra, S., Ravishankar, K., &Jayachitra, A. GreenSynthesisof silver nanoparticles using *Cassia fistula* leaf extract and its applications. *Mintage Journal of Pharmaceuticals & Medical Sciences*, 2014,20-21.

[28] Irshad, M., Zafaryab, M., Singh, M., &Rizvi, M.Comparative analysis of the antioxidant activity of *Cassia fistula* extracts. *International journal of medicinal chemistry*, *2012*.