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# *Abelmoschus esculentus* (Okra) potential natural compound for prevention and management of Diabetes and diabetic induced hyperglycemia: Review

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**Abstract**
The objective of this review is to evaluate the potential of *Abelmoschus esculentus* as a dietary agent in treatment of diabetes induced hyperglycemia. A comprehensive search of animal studies, human studies, and in-vitro assays published in scientific databases like Medline, Hub med, and printed manual scripts on herbal medicines in alternative medicine. Animal studies and in-vitro studies conducted have proved that *Abelmoschus esculentus* in form of Seeds, Peal, water soluble extracts and ethanol extracts demonstrated statistically and clinically significant results in lowering the blood glucose levels when compared to placebo, no treatment, and first line diabetic drugs like glibenclemide, metformin. Literature also confirmed the preventive effects of *Abelmoschus esculentus* on chronic diseases due to antioxidant effect exerted by high contents of natural flavonoids. Myricetin a commonly found flavonoid from *Abelmoschus esculentus* has shown protective effect in diabetes associated nephropathy, glaucoma and cataract. *Abelmoschus esculentus* can prevent and manage hyperglycemia, ingested regularly as a dietary supplement. Regular inclusion of *Abelmoschus esculentus* in daily diet (3 times in a week) can provide effective protection against diabetes and diabetic induced hyperglycemia.

**Keywords:** Abelmoschus esculentus, Okra, Diabetes Mellitus, Diabetic Nephropathy

## 1. Introduction
Diabetes is a chronic health disease attributed to risk factors like obesity, physical inactivity, ageing, genetic predisposition [1]. Type II diabetes in particular is associated with increased insulin resistance in body, causing major health complications, like heart disease, kidney damage, blindness, amputations of the legs and feet, and periodontitis [1]. On the basis of elevated blood glucose level the global prevalence of diabetes is 10% in adults aged 25+ [2]. Globally 1.3 million deaths were reported due to diabetes and related complications [2]. Low and middle income countries (LMIC's) like India, China, Brazil, have reported increased prevalence of diabetes compared to high income countries and diabetes accounts for 4% mortality caused by non-communicable diseases [2]. The primary objective of diabetes management is to maintain blood glucose level to prevent diabetes induced complications [1]. Pharmacological management includes agents that stimulate insulin secretion (sulphonylureas), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (alpha-glucosidase inhibitors) or improve insulin action (thiazolidinediones) [3]. Although Metformin is the first line drug in diabetes management, it however induces glucose intolerance. Largely pharmacologic agents fail to substantially alter the rate of progression of hyperglycemia in long run [3], thus failing to prevent progress of systemic complication arising from uncontrolled blood glucose levels [4]. *Abelmoschus esculentus* commonly known as Okra or Lady Finger is popular all over the world as a vegetable for its nutritional values and health benefits [5]. Traditionally, it has been used as an alternative treatment for diabetes [5] and when taken regularly as a part of diet has shown protective effect against Diabetes and other CHDs [6]. Here we present *Abelmoschus esculentus*, as a dietary supplement in reducing the blood glucose level in hyperglycemia induced by diabetes

## 2. Materials and methods
We searched online databases Medline, Hub med using key words like "*Abelmoschus esculents, Okra, Abelmoschus, Lady finger, Okra extracts, and Gumbo in combination with Diabetes Mellitus, DM, Type II Diabetes, NIDM, Non-Insulin Dependent Diabetes, Diabetes Insipidus, Diabetes induced hyperglycemia*". We further enhanced our search for terms like Myricetin, Quercetin to describe our intervention. The articles was limited to English language with no date limitations for search. Furthermore, we hand searched some Alternative medicine texts for literature on Medicinal Uses of Okra in Diabetes management.

We also searched in Drug Bank and Chem Hub for proteins, target proteins, pathways of the chemicals like Mycertin which are supposed to be main medicinal compound in *Abelmoschus esculentus*. Apart from these, we looked in the references of searched articles to find out relevant articles for the review. The search yielded 48 articles on the basis of key words used. 15 articles were not related to *Abelmoschus esculentus*, 2 duplicates were present, and 8 articles which did not match inclusion criteria were excluded from this review. Thus, a total of 23 articles were included in this review.

## 3. Results & Discussion

*Identification of Potential Anti-Diabetic Molecules and their targets in Abelmoschus esculentus*- A study published in 2014 described various medicinal herbs comprehensively based on the following criteria: active compounds, target proteins, pathways, investigating biological basis of pharmacological actions and chemical basis of pharmacological action. This comprises fifteen medicinal plants which were listed in "Ayurveda" for anti- diabetic effect which also includes *Abelmoschus esculentus*. Oleanolic acid, Beta Sistostenol, Myricetin, Kaempferol are the four main compounds which play role in exhibiting anti- diabetic effect brought by *Abelmoschus esculentus* (Table 1.). Myricetin is well studied and commonly found in multiple plants and has shown diverse effects such as - anti-hyperglycemic, anti – hyperlipidemia, protective effect against cardiac diseases, it has also been noted to have anticancer effect. The protective effect of Myricetin is exhibited by its antioxidant effect and free radical scavenging effect. This property is also seen in *Abelmoschus esculentus* extracts in In-vitro assay [7]. Kaempferol is another flavonoid found in *Abelmoschus esculentus* it also exhibits antidiabetic effect, protective effect against chronic disease like IHD, hyperlipidemia. It has also documented to have protective effects against various cancers. Although the protective effect exhibited by Kaempferol is mostly found statistically and clinically insignificant [8]. Oleanolic acid occurs in most edible plants and food. It has proven to have antidiabetic activity along with hepato-protective and anti-tumor outcomes. But the effect is easily reversible and binding affinity to the site is very weak [9]. Beta Sistostenol although blocks the protein targets for diabetes, but fails to show desired effects in chemical analysis. Beta Sistostenol needs to be explored further as an active compound against diabetic targets [9].

### 3.1 Animal Studies

The animal studies conducted on *Abelmoschus esculentus* can be broadly classified into Animal studies where extracts of *Abelmoschus esculentus* and the one where Myricetin was extracted from *Abelmoschus esculentus* or Synthesized Myricetin. We reviewed Animal studies according to the "ARRIVE guideline for reporting animal studies" [10] and verified for the quality of studies in terms of Methodology, Ethical conduct, Statistical analysis. The detailed analysis of the quality of the studies reviewed is presented in Table 2. The animal studies can be broadly classified based on the intervention arm as the studies with *Abelmoschus esculentus* as the intervention and the studies with Myricetin as an intervention. The studies conducted in streptozotocin-induced diabetic rats have shown that the Okra extracts including peel extracts and seed extracts given water soluble solution can effectively lower the blood glucose level up to 10% (75mg/dl) in diabetic control arm and when compared to reduction brought by glibenclemide 5mg, *Abelmoschus esculentus* was able to bring the further reduction in blood glucose by 5% (15gm/dl). While looking at the time required to bring the reduction in blood glucose level *Abelmoschus esculentus* was able to reduce the glucose level from 4.7mmol/L at 2hrs to 3.8mmol/L at 4hrs as compared to glibenclemide where reduction was from 4.7mmol/L at 2hrs to 4.0mmol/l at 4hrs. [11] *Sabitha et al. 2011 Jul* [12] *Fan et al. 2014 Jul* [5] *Khatun et al. 2011* [13] *Tian et al. 2015 Dec.* The study conducted by [5] Khatun et al. has demonstrated that *Abelmoschus esculentus* has antagonist effect on metformin. *Abelmoschus esculentus* extracts when co-administered with metformin, lead to loss of effect of metformin (33.5 to 32.2mmol/L at 4hrs).

The studies which used Myricetin as an intervention have used no treatment control arm wherein the myricetin effect was seen inflamed. Myricetin was able to bring down the blood glucose level by 50% in streptozotocin-induced diabetic rats from 160.7 ± 7.0mg/dl to 149.6 ± 6.2mg/dl ($P < 0.05$) at the rate of 3mg/hr. over a period of 12 hrs. [14] *Choi et al. 2014 Oct* [15] *Ong et al. 2000 Aug* Myricetin has also shown protective effect nephrotic disorders in rats. [16] *Ozcan et al. 2012 Dec* Myricetin improves carbohydrate metabolism and enhances glucose utilization. [17] *Kandasamy et al. 2014 Sep.*

*Human Studies* - Human studies on effects of *Abelmoschus esculentus* in management of diabetes mellitus have not been conducted. There are few studies which collectively study the effect of bioflavonoids on CHD's, these bioflavonoids includes Myricetin, Kaempferol present in various natural sources including *Abelmoschus esculentus*. A lower risk of type 2 diabetes tended to be associated with high intakes Quercetin (RR: 0.81; 95% CI: 0.64, 1.02; P = 0.07) and Myricetin (0.79; 0.62, 1.00; P = 0.07), as per follow up study done on 10054 Finnish men and women for 2 years [8]. But the effect size was small and was not statistically significant with both Quercetin and Myricetin. Another prospective study conducted on 38,108 women aged 45 or more, free from cardiovascular diseases, cancer, and type II diabetes, reported after 8.8 years average follow-up the relative risk of type II diabetes (RR : 0.75, 95% CI: 0.56, 0.92: P = 0.006) when women consuming flavonoid rich food was compared with women not consuming flavonoid rich food.[18]. One cross sectional study conducted amongst 500 type II diabetic patients in Africa to demonstrate protective effective of antioxidant rich Mediterranean diet in reducing the risk of blindness, cataract, and glaucoma in type 2 diabetic patients. Demonstrated that regular intake of *Abelmoschus esculentus* reduces risk of blindness (n- 9, 18%) cataract (n-2, 4%) glaucoma (n-1, 2%) as compared never intake of *Abelmoschus esculentus* where blindness (n-60, 76.9%) cataract (n-34, 43.6%) glaucoma (n-24, 30.8%) with P value <0.05. Followed for 6 months [6]. Human studies though reported protective effect of *Abelmoschus esculentus* consumption on type II diabetes and related complication, the studies were observational in nature so were unable to explain the true protective effect.

### 3.2 Tables and Figures

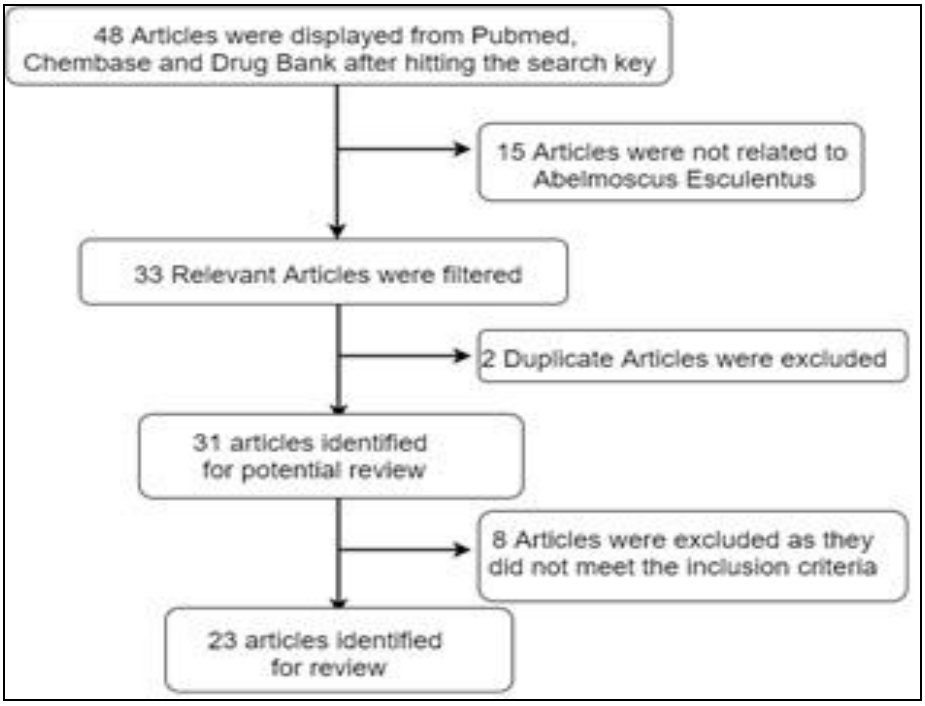


**Fig 1:** study flowchart

**Table 1:** Protein targets of the active compounds

| Active Compounds | Protein Targets |
|---|---|
| Beta Sistostenol | 5-alpha reductase |
| Oleanolic acid | COX 2<br>COX 1<br>Diacylglycerol acyltransferase<br>DNA Polymerase beta<br>Gaba transaminase<br>Glycogen phosphorylase |
| Myricetin | Alpha amylase<br>Xanthine oxidase<br>PI3K<br>Insulin receptor |
| Kaempferol | Aldose reductase<br>Lipoxygenase |

**Table 2:** Reporting of Animal studies according to ARRIVE guidelines

| Study Author | Animal under investigation | Randomization | Sample Size | Control type |
|---|---|---|---|---|
| Sabitha et al. | Streptozotocin-induced diabetic rats. | Not done | 42 | Standard Control (glibenclemide) and No treatment control |
| Fan et al. | high-fat diet-induced obese C57BL/6 mice | Simple randomization | 12 | No treatment control |
| Khatun et al. | Long Evans Rats | Simple randomization | 60 | Standard Control (metformin) and Not treatment control |
| Choi et al. | Streptozotocin-induced diabetic rats. | Simple randomization | 28 | No treatment control |
| Ozcan et al. | Male Albino Wister Rates | Not done | 48 | No treatment control |
| Ong et al. | Streptozotocin-induced diabetic rats. | No information available | 30 | No treatment control |
| Kandasamy et al. | Streptozotocin-induced diabetic rats. | No information available | 24 | No treatment control |

## 4. Conclusions

*Abelmoschus esculentus* may be considered as an important component of preventive therapy in management of type II diabetes and its associated complications. The main bioactive constituent of A. esculentus is Myricetin and notable work has been done to explore its protective effects in various CHD's and cancers. Literature also investigates the effect of antioxidants like natural flavonoids on diabetes and CHDs. Animal studies which involve *Abelmoschus esculentus* were statistically able to prove the blood glucose lowering effect in STZ induced diabetic rats. Human studies also demonstrated protective effect but the effect size is not large.

Data pertaining toxicity and adverse effect in both animal and human studies after intervention with *Abelmoschus esculentus* in any form extracts, powder, alcohol extracts, and water soluble extracts was scarce and mostly not documented. There

is sufficient data which demonstrates the efficacy of *Abelmoschus esculentus* in management of type II diabetes mellitus and its complications using animal models as compared to data on safety and toxicity. Along with well documented literature on active compounds present in *Abelmoschus esculentus* and their protein targets and pathways involved. Hence *Abelmoschus esculentus* has a potential to serve as therapeutic agent in management of type II diabetes and its complications but needs exploratory human clinical trials do initiate the process.

Thus we would recommend, that *Abelmoschus esculentus* should be subjected to early phase human clinical trials as a dietary supplement for studying the protective effect on human subjects in controlled conditions. We also suggest that the *Abelmoschus esculentus* or Okra fruit should be used as a whole as Active Pharmaceutical Ingredient (API) in this scenario instead of using chemical extracts like Myricetin or Kaempferol as an API. Using *Abelmoschus esculentus* fruit as API will help to understand the protective dietary benefits of this plant, which can be further extended to seeds, peel or water soluble extracts to investigate in Pragmatic human trials.

Conflict of Interest - None

## 5. References


1. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention. Diabetes Report Card 2014. Atlanta, GA: Centers for Disease Control and Prevention, US Dept. of Health and Human Services; 2015. [Internet]. Atlanta, GA 30341-3717: Centers for Disease Control and Prevention, US Dept. of Health and Human Service; 2015 [cited 2016 Oct 11]. (Diabetes Report Card 2014). Available from: www.cdc.gov/diabetes/library/reports/congress.html
2. World Health Organisation. Global status report on NCDs 2010. In Genneva, Switzerland; [cited 2016 Oct 17].1:23. (Non communicable diseases; vol. 2010). Available from: http://www.who.int/entity/nmh/publications/ncd_report_chapter1.pdf?ua=1
3. Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. Drugs. 2005; 65(3):385-411.
4. Pelikanova T. [Treatment of diabetes in metabolic syndrome]. Vnitr Lek. 2009; 55(7-8):637-45.
5. Khatun H, Rahman A, Biswas M, Islam AU. Water-soluble Fraction of Abelmoschus esculentus L Interacts with Glucose and Metformin Hydrochloride and Alters Their Absorption Kinetics after Co administration in Rats. ISRN Pharm. 2011, 260537.
6. Moise MM, Benjamin L-M, Doris TM, Dalida KN, Augustin NO. Role of Mediterranean diet, tropical vegetables rich in antioxidants, and sunlight exposure in blindness, cataract and glaucoma among African type 2 diabetics. Int. J Ophthalmol. 2012; 5(2):231-7.
7. Kilkenny C, Browne W, Cuthill IC, Emerson M, Altman DG. Animal research: reporting in vivo experiments: the ARRIVE guidelines. Br J Pharmacol. 2010; 160(7):1577-9.
8. Gul MZ, Bhakshu LM, Ahmad F, Kondapi AK, Qureshi IA, Ghazi IA *et al.* Evaluation of Abelmoschus moschatus extracts for antioxidant, free radical scavenging, antimicrobial and antiproliferative activities using in vitro assays. BMC Complement Altern Med. 2011; 11:64-64.
9. Knekt P, Kumpulainen J, Jarvinen R, Rissanen H, Heliovaara M, Reunanen A, et al. Flavonoid intake and risk of chronic diseases. Am J Clin Nutr. 2002; 76(3):560–8.
10. Fayaz SM, Suvanish Kumar VS, Rajanikant KG. Finding Needles in a Haystack: Application of Network Analysis and Target Enrichment Studies for the Identification of Potential Anti-Diabetic Phytochemicals. Ahmad M, editor. PLoS ONE. 2014; 9(11):112-911.
11. Sabitha V, Ramachandran S, Naveen KR, Panneerselvam K. Antidiabetic and antihyperlipidemic potential of Abelmoschus esculentus (L.) Moench. In streptozotocin-induced diabetic rats. J Pharm Bioallied Sci. 2011; 3(3):397-402.
12. Fan S, Zhang Y, Sun Q, Yu L, Li M, Zheng B, *et al.* Extract of okra lowers blood glucose and serum lipids in high-fat diet-induced obese C57BL/6 mice. J Nutr Biochem. 2014; 25(7):702-9.
13. Tian Z-H, Miao F-T, Zhang X, Wang Q-H, Lei N, Guo L-C. Therapeutic effect of okra extract on gestational diabetes mellitus rats induced by streptozotocin. Asian Pac J Trop Med. 2015; 8(12):1038-42.
14. Choi H-N, Kang M-J, Lee S-J, Kim J-I. Ameliorative effect of myricetin on insulin resistance in mice fed a high-fat, high-sucrose diet. Nutr Res Pract. 2014; 8(5):544-9.
15. Ong KC, Khoo HE. Effects of myricetin on glycemia and glycogen metabolism in diabetic rats. Life Sci. 2000; 25:67(14):1695–705.
16. Ozcan F, Ozmen A, Akkaya B, Aliciguzel Y, Aslan M. Beneficial effect of myricetin on renal functions in streptozotocin-induced diabetes. Clin Exp Med. 2012; 12(4):265-72.
17. Kandasamy N, Ashokkumar N. Protective effect of bioflavonoid myricetin enhances carbohydrate metabolic enzymes and insulin signaling molecules in streptozotocin-cadmium induced diabetic nephrotoxic rats. Toxicol Appl Pharmacol. 2014; 1,279(2):173-85.
18. Song Y, Manson JE, Buring JE, Sesso HD, Liu S. Associations of dietary flavonoids with risk of type 2 diabetes, and markers of insulin resistance and systemic inflammation in women: a prospective study and cross-sectional analysis. J Am Coll Nutr. 2005; 24(5):376-84.