Does Abelmoschus Esculentus act as anti-diabetic? A scoping review with updated evidence

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Abstract

Background: It is well known that Diabetes Mellitus is one of the leading causes of morbidity and mortality arising from multiple etiologies and still is an incurable one. Besides modern medicines and technologies, science is looking at some nature made remedies to avoid toxic side effects and to invent a hassle-free treatment for it. While plant resources have turned into a chief target to search new drugs, Abelmoschus Esculentus is claimed to be an alternative approach to current medicines of diabetes but yet need to explore more.

Methods (Search strategy): Review authors searched PubMed, Medline, Embase, CINAHL, Scopus database (last search July 30, 2020), with the MeSH terms and keywords of Abelmoschus Esculentus, lady's finger, and Diabetes mellitus to make a brief explanation regarding effects of Abelmoschus Esculentus on diabetes, along with summary of molecular evidence, nutritive and phytochemical components, illustrative evidence of human trial and mice demonstration. Selected articles are also screened in the reference list to find other relevant content.

Expected outcome: This review can highlight the current evidence of the particular topic, useful for a reader to gain knowledge, application in clinical practice in a community setting, or planning for new human experiment in depth.

Keywords: Abelmoschus Esculentus, Lady's finger, Okra and Diabetes mellitus

Introduction:

Diabetes mellitus is a progressive metabolic disease that affects a significant percentage of the population (estimated to be 9.3%, 2019) throughout the world [1]. Though various types of diabetes have different pathogenesis, hyperglycaemia and its related symptoms are common for all. If left untreated, diabetic complications lead to mortality because of numerous pathophysiological changes. Presently, diabetes is managed or controlled by pharmacological agents in addition to some of the non-pharmacologic approaches, such as exercise and diet [2]. However, all of the modern drugs don't cause adverse effects but now the scientific community is engaged in a search for new molecular compound from all possible sources, including Ayurveda, natural herbs, or any other traditional medicines that might be less toxic when compared with existing treatment remedies. Abelmoschus Esculentus has seemed a potential answer to the challenge of the present medical system for treating diabetes. [3] Abelmoschus Esculentus or Lady's finger or Okra is a perpetual flowering houseplant belongs to the Mallows or Malvaceae family, grown as summer vegetables throughout tropical and sub-tropical region of the world [4]. From historical perspectives, Kew Royal Botanic Gardens UK, declared about Okras' cultivation by people in Egypt as long ago as 2000 B.C. [5]. Now, it is the most common vegetable of every day's diet of the individuals from Southern Europe, America, and Africa to Asia, [6]. Yet, it is renowned as a laxative, demulcent, emollient poultice, treatment of jaundice, gastric irritation, and many more [4, 7, 8]; but the potentiality to stabilize blood sugar is not that much highlighted and well documented. Hence, the present review is aimed to investigate as well as explore its anti-diabetic properties with scientific data, revealed literature, and current evidence.

Methods (Search strategy):

Using PRISMA guidelines, we searched PubMed, Medline, Embase, Ovid, Discovery search, Delnet, Clinical key, and Cochrane Trials Register along with some hand search for finding studies eligible for this review. Keywords, Free-text terms and Mesh terms such as "Abelmoschus Esculentus" OR "Okra" OR "Lady's finger"; "Abelmoschus Esculentus AND Serum blood glucose"; "Abelmoschus Esculentus AND Type 2 Diabetes Mellitus"; "Abelmoschus Esculentus AND Anti-diabetic"; " Okra AND Type 2 Diabetes Mellitus"; "Okra AND serum blood glucose"; "Okra AND Antidiabetic"; "Lady's finger AND Type 2 Diabetes Mellitus"; "Lady's finger AND Anti-Diabetic"; " Lady's finger AND Serum blood glucose" were used for the purpose. Two reviewers searched, examined the eligibility of the studies independently. We also reviewed cross-references cited in retrieved articles to identify additional relevant studies. The discrepancy among the two reviewers was resolved through discussion with the primary reviewer.

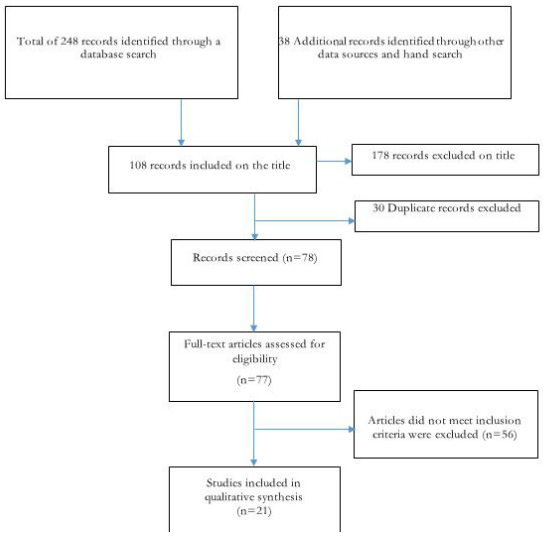
Study Selection:

We selected studies, which were fulfilling the following criteria:

- Studies examining the effectiveness of Abelmoschus Esculentus on Type 2 Diabetes Mellitus through its genetic pathway.
- Studies examining Abelmoschus Esculents' phytochemical and biological components that work against diabetes.
- Studies examining the relationship between Abelmoschus Esculents and serum blood glucose, glycosylated haemoglobin and other biomarkers of Type 2 Diabetes in mice and human trial
- Studies published in the English language.
- All experimental and observational studies till the date of search.
- We excluded the studies or papers:
- Case reports, letters, editorials, opinions, commentaries, review papers
- Studies on other properties or biological values of Abelmoschus Esculents instead of its anti-diabetic role

Data Extraction:

We performed a literature search till July 30, 2020, as per the PRISMA guideline (Figure-1). A total of 266 studies were identified by using a different database (PubMed-36, EMBASE-61, Ovid- 45, Discovery Search- 85, Clinical Key-2, Cochrane Library and Clinical Trial-19 respectively while 18 studies were from a hand search and search from other databases). We identified 21 studies that fulfilled the eligibility criteria of our review. All of them are true experimental studies, clinical trials both human and animal. There is no published randomized controlled trial on humans with a large sample size to advocate Abelmoschus Esculentus as anti-diabetic.



Data Synthesis and Analysis

Finally, 21 studies were found suitable for consideration in writing this comprehensive evidence-based rapid review. Data regarding selected

variables were extracted from each included study as per the objective of this review, categorized and then tabulated [Table- 1, 2 and 3] in a simple way to communicate the results. Meta-analysis was not done because of clinical and methodological heterogeneity among the included studies. Therefore, the narrative summary approach was used for data synthesis. The qualitative synthesis was carried out from extracted data but the quantitative analysis couldn't be performed between the studies.

Table: 1 Major Phytochemicals extracted from Abelmoschus Esculentus and its anti-diabetic role

	activated receptors) and LXRs (liver X receptors) along with their target protein sequence in adipose tissue and liver of the model diabetic rats. These results suggested therapeutic effects of okra polysaccharide on metabolic diseases via inhibiting the signalling of LXR and PPARs [13].
Polyphenols (quercetin, catechins oligomers and hydroxycinnamic derivatives)	Polyphenol-rich diets are inversely correlated to the incidence of type 2 diabetes [14]. Bioactive polyphenols of okra (quercetin, catechins oligomers and hydroxycinnamic derivatives) regulate signalling pathways as insulin mimic to exert metabolic effects[16].
Isoquercetin and quercetin-3-O-beta-glucopyranosyl-glucoside (type of flavonolglucosides)	There is presence of α-glucosidase inhibitors in okra seeds [17]. Alpha-glucosidase is an intestinal enzyme responsible for breaking down of carbohydrates. Potential inhibition of enzymes α glucosidase and α amylase by Abelmoschus esculentus aqueous extracts (peel and seed powder) in vitro study confirmed the hypo-glycaemic effect [18].
Gallic acid and Quercetin	Abelmoschus esculentus down-regulated expression of PPARs gene in pancreas, protein expressions of phosphorylated Akt (p-Akt), phosphorylated p38MAPK, TGF-β1, and TNF-α in the kidney. In addition, it improved islets structure when examined on diabetic nephropathy model rats [19].
Total Flavone Glycoside from Okra Fruit	TFGO obtained from ethanol extract of okra by column chromatography has significant antidiabetic potential which was measured by comparing body weight, fasting blood glucose, oral glucose tolerance test (OGTT), superoxide dismutase (SOD), malonaldehyde, triglycerides, total cholesterol, organ index, and histological section of renal tissue in diabetic model rats [20].
Pentacyclic triterpene ester, quercetin glucosides, carbohydrates, polysaccharides	Lipo-toxicity plays an important role in exacerbating T2DM and leads to apoptosis of β cells. Abelmoschus esculentus subfractions prevent free fatty acid induced β cell apoptosis via inhibiting dipeptidyl peptidase 4 [21].
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Table: 2 Animal trials with clinical outcomes to support the effects of A. Esculentus on Diabetes

Authors	*Subjects of the experiment*	*Treatment*	*Results*
Indah Mohd Amin [22]	Analysis of gene expression in liver tissue in STZ induced diabetic rat Selected diabetes-specific genes were: 1. Caboxyl esterase 2 2. Stearoyl Coenzyme a desaturase 1 3. Insulin like growth factor 1 4. Insulin like growth factor binding protein 2	Oral application of water extract of AE at doses of 100, 150, 200 mg/kg body wt.	RNA extraction for gene expression analysis was done by RT-PCR method. The abnormal expression of diabetics specific genes were rescued by A. esculentus therapy.
Agnes J X et al.[23]	Serum blood glucose in Alloxan monohydrate induced Male Albino Wister strain rats Serum glucose above 200mg/dl was considered as diabetic	Oral feed of AE Plant extract of (150mg/kg bwt) & Glibenclamide (5mg/kg bwt) for 12 days	At the end of the expeiment:: Normal rats 74.3±0.5 mg/dl Diabetic Control rats 212.5±1 mg/dl Diabetic + plant extract 110.8±0.1 mg/dl Diabetic + Glibenclamide 85.4±3.9 mg/dl
V. Sabitha et al.[24]	Glycosylated haemoglobin (HbA1C) in streptozotocin-induced diabetic Male Wister albino rats	Oral feed of 0.2% Caboxy methyl cellulose (5 mL/kg) for normal & diabetic control rats; A. esculentus peel and seed powder (AEPP, AESP); Glibenclamide for diabetic expesimental rats for 28 days	At the end of expeiment:: Normal rats 7.12± 0.08 Diabetic control 13.03±0.13 AEPP 100 mg/kg 5.86±0.09 AEPP 200 mg/kg 4.98±0.12 AESP 100 6.51±0.17 AESP 200 mg/kg 6.702±0.14 Glibenclamide (5 mg/kg) 5.90±0.19 Administration of AEPP in both dose (100 and 200 mg/kg bwt) showed significant reduction of HbA1c
Huang C-N et al.[25]	Assessment of homeostasis model for insulin resistance index (HOMA-IR) in streptozotocin (35 mg/kg b wt.) induced male Sprague-Dawley rats	Oral feed of AE subfractions (F2) which contains carbohydrates and polysaccharides for 12 weeks	Insulin resistance was reduced (from HOMA-IR 9.8–13.8 to HOMA-IR: 5.3) at the end of 12 weeks
Esfani Majd N et al.[19]	Lipid profile in HFD-STZ-induced diabetic adult female Wistar rats.	Oral feed of A. esculentus powder at 200 mg/kg body weight for 30 days	At the end of expeiment:: Diabetic control / Diabetic AE Triglyceride 93.22 ± 25.12 / 52.83 ± 1.92 T. Cholesterol 140.13 ± 19.5 / 98.89 ± 5.02 LDL 91.15 ± 18.17 / 63.79 ± 4.87 HDL 22.03 ± 3.04 / 22.93 ± 1.01 Insulin 47.9 ± 3.2 / 62.06 ± 3.96 HOMA- IR 21.77 ± 1.45 / 17.8 ± 4.47
Sabitha V et al.[24]	Biomarkers of antioxidants was investigating parameters Diabetes was persuaded by STZ injection (60 mg/kg).	Diabetic rats received A. esculentus seed and peel powder (100 and 200 mg/ kg) orally till 28 days.	Administration of A. Esculentus (seed and peel powder) augmented kidney, liver, as well as pancreas superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione (GSH), catalase (CAT) in addition to diminished thio barbituric acid reactive substances (TBARS) in diabetic rats compared to control group which confirmed in vivo antioxidant property of A. esculentus in diabetes.
Yang LW et al.[27]	Enquiry on neuro-protection of A. esculentus against diabetic neuropathy in Alloxan monohydrate induced diabetic male Sprague Dawley albino rats. Sciatic nerve tissues were studied for histopathological investigation.	A. esculentus L. ethanol extract at a dose of 100 and 200 mg/kg of bwt in single dose per day till 21 days.	Results showed significant decrease in blood glucose and thermal hypoalgesia and increase in rotarod performance of muscle grip strength. The sciatic nerve fiber of diabetic rats receiving A. esculentus L. extract showed no swelling, and lesser demyelination.

Results:

Using a narrative approach this review has discussed the role of various phytochemical components present in Okra as anti-diabetic, evidence of their pathways over the diabetic gene along with its clinical efficiency in human and mice trial. There are several studies performed in true scientific settings on the diabetic gene of model rats received the positive effects of Abelmoschus Esculentus in the insulin signaling pathway are listed below in Table -1. Animal studies with major findings that confirm changes in response in the clinical outcome such as serum blood glucose, glycosylated haemoglobin, biomarkers of type 2 diabetes mellitus after providing alcohol or aqueous extract of Abelmoschus Esculentus are listed below in Table -2. Although, there are very few human trials had conducted on this particular topic but most authentic trials with their methodology and measuring variables of diabetes are listed below in Table- 3.

Author	*Methodology*	*Results*
Sasika Davis et al, 2014, Mangalore[28]	***Research design:*** quasi-experimental approach with purposive sampling technique ***Population:*** patients with Type 2 diabetes aged 45-60 years. ***Sample size:*** 40 ***Treatment:*** lady's finger juice ***Outcome variable:*** fasting blood glucose	Mean FBG value of the experimental group was in the pre-test (219.3±69.3), post-test 1 on 7th day (199±67.9) and post-test 2 on the 11th day (189.45±67.2) which confirmed significant decline in FBG value in the experimental group. Control group had no change in mean FBG value.
Shobana B. 2016. Dharapuram[29]	***Research design:*** quasi-experimental pre-test post-test design with purposive sampling technique ***Population:*** patients with Type 2 diabetes ***Sample size:*** 60 ***Treatment:*** lady's finger juice ***Outcome variable:*** fasting blood glucose	The mean pre-test value of FBG was 178 (SD± 43.1), mean post-test 1 value on the 7th day was 135 (SD±19.2) and post-test 2 mean value on the 16th day was 107 (SD ± 13.01). Control group had no change By applying independent and paired t test study findings revealed significant difference between means which showed good potential of okra as anti-diabetic (p value <0.05).

Table: 3 Evidence of human trials on the effects of Abelmoschus Esculentus on Diabetes

Discussion:

As per National Nutrient Database of the USDA (U.S. Department of Agriculture)[30], one tea cup of uncooked fresh lady's finger, considering around 100 grams contains calories 33 g, protein 1.93 g, fat 0.19 g, fiber 3.2 g, carbohydrate 7.45 g, sugar 1.48 g, vitamin K 31.3 mg, vitamin A 36 mcg, thiamin 0.2 mg, vitamin B6 0.215 mg, vitamin C 23 mg, potassium 299 mg, magnesium 57 mg, sodium 7 mg, calcium 82 mg and 60 mcg of folate along with some iron, phosphorus, and copper. According to the American Diabetes Association, non-starchy vegetables with minimal glycemic index can be freely enjoyed by diabetics. Therefore, Abelmoschus Esculentus is a decent choice for people living with diabetes, as it has a very low glycaemic index nearby 20 [5].

- Studies have been revealed its vitamins (niacin, riboflavin, ascorbic acid, tocopherol and carotenoids), polyphenols (rutin, procyanidins, catechins, and epigallocatechin), polysaccharides (gum, pectin, cellulose, and hemicellulose) and flavonoids (quercetin isomers) impending chemo protective effects as hypolipidemic, antidiabetic, neuroprotective, and anti-fatigue (by Agnes Jenitha X et al, Fatemeh Akbari et al,) [23, 31]. In an in-vitro study, Khatun HM et al investigated potential of viscous soluble dietary fibre (VSDF) of okra (Abelmoschus Esculentus L) in dropping absorption of intestinal glucose and found out substantial reductions of diffusion of glucose from the water-soluble portion of the pods of Abelmoschus Esculentus L [32]. Diffusion systems implicates a possible potential ($P<0.05$) when comparing to control in a concentration dependent manner.

- Among diabetics, the increased free radicals were observed. Oxidation of glucose, glycation of proteins, and oxidative degradation of glycated proteins are blamable for the formation of oxygen free radicals which plays a major role in the development of diabetic complications. Therefore, any natural resources filled with antioxidant is useful for diabetes [26]. Administration of subfractions of A. Esculentus improved kidney, liver, and pancreas SOD, GPx, GSH, CAT levels and diminished TBARS levels in model diabetic rats which confirmed significant in vivo antioxidant property of it. Primarily flavonoids (phenolic structure) and polysaccharides (Large structure of carbohydrate) present in ethanolic or water extract of Abelmoschus Esculentus works in different pathways of the diabetic gene which compensates insulin deficiency or improper utilization of it. Among those, muscle GLUT 4 gene expression[10], hepatic PEPCK gene expression[10], type 1 glucagon-like peptide receptor and dipeptidyl peptidase 4 signalling pathway[11], AMPK-Sirt1-PGC-1α

signalling axis [13], PI3K/ AKT/ GSK3β pathway [14], the Nrf2 expression [14], gene expression of LXRs and PPARs [15], protein expressions of phosphorylated Akt (p-Akt), phosphorylated p38MAPK, TNF-α, and TGF-β1 [19] are significant. Decreased insulin sensitivity or insulin resistance is key factor of diabetes pathophysiology where inability of insulin to perform in glucose uptake, utilization, metabolism and storage had been observed. At molecular level occurrence of mutation or post-transitional modification at insulin receptor or its downstream effector molecule are the blamable one. Above studies revealed about rescue of those gene receptor and their target compound after okra therapy comparable with metformin or other sulfonylurea.

-As a natural herb, Abelmoschus Esculentus don't have any toxic adverse effect and any negative feedback mechanism. Not only in pathway mechanism, this insulin mimic, and low glycemic index fruits has also shown its antidiabetic effects in numerous clinical outcome e.g. fasting blood glucose, HbA1c, triglycerides, total cholesterol, high and low-density lipoprotein, HOMA-IR and insulin resistance [22-27]. Though the screened phytochemical compound in ethanolic and aqueous extract of Abelmoschus Esculentus has ascertained its medicinal value and significant therapeutic uses as herbs [33-35] all those mechanism studies and computational docking had done on mice, causing lack of data on human. Therefore, Randomized clinical trial on patients with Type 2 diabetes mellitus is recommended to investigate the anti-diabetic effects of Abelmoschus Esculentus on humans with proper evidence in depth.

Conclusion:

The findings of the present systematic review had revealed the anti-diabetic properties of okra. Outcomes from in vivo, molecular studies, and trials suggested that the plant extract of Abelmoschus Esculentus can be used for the management of the disease. As diabetes mellitus is forecasted to be a very major disease by the year 2030, there is a pressing need to explore better remediation, research in-depth to be brought it as anti-diabetic in the form of synthetic or natural.

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Conflict of interest: There is no conflict of interest

Ethical statement: This review does not include animals' and humans' participation. Therefore, ethical approval is not needed.

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