WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 3, 312-324. Research Article ISSN 2277– 7105

THE THERAPEUTIC EFFECT OF ABELMOSCHUS ESCULENTUS (OKRA) ON RATS INDUCED DIABETES THAT THROWS NEW LIGHT ON MANAGING TYPE II DIABETIC PATIENTS

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Article Received on
10 Jan. 2019,

Revised on 31 Jan. 2019,
Accepted on 20 Feb. 2019

DOI: 10.20959/wjpr20193-14402

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ABSTRACT

Background: Abelmoschus esculentus (Okra) is one of popular vegetable in many countries. Medically it is an excellent source of potassium, vitamins B, C, antioxidants and calcium. Nowadays it becomes an area of interest due to its antidiabetic effect. In this systematic review we are using mice to model human disease. Genetically and gnomically, the human and the mouse are very similar, with many of the disease-related genes are nearly identical. The major objective of this study was to investigate the therapeutic effect of Abelmoschus esculentus (okra) on diabetic mice, and the impact of the outcome results on type II diabetic patients. **Method:** PubMed, Cochrane databases, Access Medicine and Google Scholar search was conducted to find out studies that evaluate the ability of Okra to lower blood glucose on diabetic mice. As the result of the deep search and using inclusion and exclusion criteria and JBI critical appraisal tools 4 articles were selected. All of these articles evaluate the antidiabetic effect of Okra. **Results:** All the identified studies confirm the antidiabetic effect of Abelmoschus esculentus in diabetic rates. The results showed clear reduction in the level of blood glucose, HbA1c and others diabetic markers. In addition to this they revealed potential of hypolipidemic, anti-inflammatory and anti-cancer effects of okra. **Conclusion:** The results of this systematic review confirm that Okra has the potential to be an excellent choice for managing glucose level on type II diabetic patients. However, direct studies on human type II diabetic patients need to be done before confirming its effect in human.

KEYWORDS: AE: Abelmoschus esculentus. **HbA1C**: Haemoglobin A1C test. **TG**: Triglyceride **HDL**: High Density Lipoprotein. **LDL**: Low Density Lipoprotein.

INTRODUCTION

Diabetes is a one of the metabolic disorders which is characterized by hyperglycemia and impaired action and secretion of insulin (WHO, 2018). It is considered a major public health problem, worldwide and it is linked with the high rate of death cases (WHO, 2018). According to WHO report in 2018, the number of people with diabetes was estimated to be about 422 million in 2014 and most of these cases occur before the age of 70 (WHO, 2018). Diabetes is the common leading cause of death in the world and can be considered as the major cause of kidney failure, heart attack, blindness and stroke (WHO, 2018). There are different types of diabetes but all of them are associated with hyperglycemia. Type 1 diabetes is called insulin-dependent diabetes because it occurs due to the problem in the secretion of insulin, the hormone that decreases blood glucose level by increasing its absorption by the body cells (WHO, 2018). on the other hand, type 2 diabetes is associated with inability of the body to use insulin effectively and it is usually called insulin-resistant diabetes (WHO, 2018). This form of diabetes is more prevalent and it is associated with the most complicated problem (WHO, 2018).

As it is increasingly recognized as a serious, worldwide public health concern, various types of medications have been manufactured for type 2 diabetes. Some of them depend on the regulation of insulin level (Panneerselvam et al., 2011). However, these medications have many limitations and can cause many side effects (Katherine Marengo LDN, 2019). Therefore, the natural, traditional treatments are the best choice for many (Katherine Marengo LDN, 2019).

Many studies have revealed that type 2 diabetic patients can control their condition from getting worse by making a change in their lifestyle and diet. Medications cannot be effective without dietary change and exercise (Katherine Marengo LDN, 2019). Making a change in lifestyle is the common suggestion to keep the blood glucose low and to prevent the serious complications of diabetes according to many studies (Katherine Marengo LDN, 2019). There are various natural foods which are medically recommended to be included in diabetic patients dietary (Suzanne Falck, 2019). These foods include sweet potatoes, oatmeal, oat bran, most nuts, legumes, garlic and okra (Katherine Marengo LDN, 2019).

Nowadays, the natural and traditional medications are a major area of interest within the field of typ2 diabetes and there are many studies focused on natural recourses to manage the level of blood glucose instead of the manufactured medication which can lead to many side effects (Katherine Marengo LDN, 2019).

Abelmoschus esculentus fruit (Okra) is one of traditional choice to keep the blood glucose low (Muhammad et al., 2017). It is a type of vegetable which can grow in almost all counties but more concentrated in Africa (Muhammad et al., 2017). It is known as lady's finger in many English-speaking countries. Medically It is a valuable vegetable because it contains potassium, vitamins B, C, fiber and calcium (Suzanne Falck, 2019). Moreover, it is rich of antioxidants which can reduce oxidative stress according to the National Center for Complementary and integrative health in the U.S (Katherine Marengo LDN, 2019). In some countries of Asia Okra is used as a traditional treatment to treat gastric irritation and usually prescribed for patients who suffer from weakness, depression, ulcer and lung inflammation (Panneerselvam et al., 2011). In addition to this, it was suggested to manage blood glucose according to a study published in 2011 in the journal of pharmacy& BioAllied science and it was included in the list of non-starchy vegetables that are benefit to diabetic patients according to the American Diabetes Association (Katherine Marengo LDN, 2019).

Many studies showed that okra possesses hypoglycemic effect in mice (Panneerselvam et al., 2011). A 2017 study published in PLOS found a substance in okra called myricetin can lower the level of blood glucose in rates by increasing its absorption in muscle (Katherine Marengo LDN, 2019).

Despite the advantages of Okra, the medical studies to prove its benefits are still in early stages and although the extensive research which has been carried out on diabetes treatment there are few were done on Okra. So, current the systematic review was aimed to investigate the antidiabetic activity in Abelmoschus Asculentus (okra) by examining available studies and scientific information to provide a clear view to the scientific community.

The method

This study systematically reviews the available data of Abelmoschus Esculentus (okra) on glucose level of mice because they are genetically very similar to humans, aiming to provide clinical evidence on type 2 diabetic patients about its ability to lower the blood glucose.

To achieve this goal a preliminary search was done on January 16, 2019 using the following data resources: PubMed, Cochrane databases, Access Medicine and Google Scholar to find out studies and scientific information that evaluate the ability of Okra to lower blood glucose in type 2 diabetes. All the studies which are published in English from 2000 to 2019 were included in the search. As the results more than 100 studies related to Abelmoschus Esculentus were found.

To make the results more accurate: the following keywords were used: antidiabetic effect of Abelmoschus Esculentus, Abelmoschus Esculentus and diabetes, Okra and antidiabetic effect. As the results of using these keywords, the number of studies reduced to less than 15. For the purpose of quality and specificity of the search the studies were excluded if there are opinion, review, text studies or Systematic review and to avoid any factors that can affect the quality of the search and to increase its efficiency we filtered the studies that we obtained using PubMed search filter, Cochrane databases search filter and EMBASE search filter. As a result of using inclusion and exclusion criteria and other methods of filtering the number of studies reduced to 6. These 6 studies were screened by examining the abstract, method and the results and finally the best 4 were selected based on the quality of the method and the results that have been found. All the selected studies evaluate the antidiabetic activity in Abelmoschus Esculentus (okra) and they have a good representation of the results.

To make sure that their methods are at the good quality we did appraise them using the JBI critical appraisal tools. The major type of checklist that is used is an experimental study checklist. By using this critical appraisal tool, we were able to find the strengths and weaknesses of each study and we concluded that the selected studies are at good quality to be used in any systematic review based on the JBI critical appraisal tools and inclusion and exclusion criteria. The process of identifying the studies is clearly summarized in figure 1.

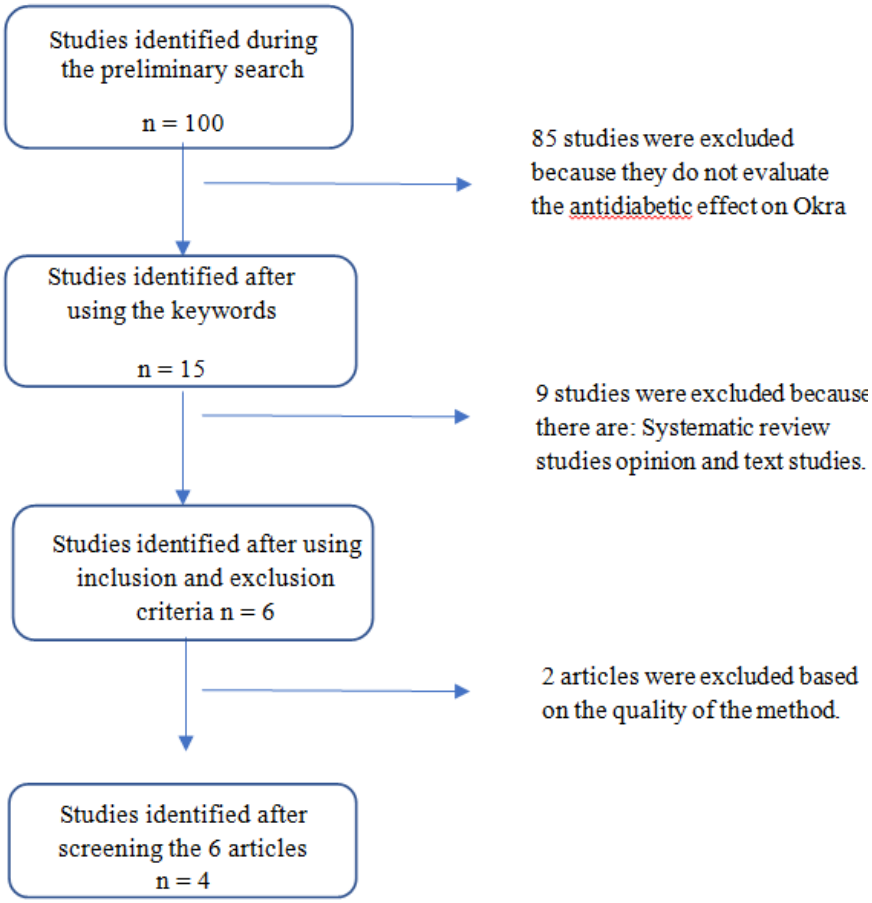

Figure1: Process of identifying the articles that evaluate the antidiabetic effect of Abelmoschus Esculentus.

THE RESULTS

The results of the assessment of the identified studies

To assess the quality of the identified studies the JBI critical appraisal checklist was used. This tool is designed to evaluate the accuracy and quality of experimental studies to identify the risk of bias. As a result of using JBI critical appraisal checklist we were able to examine the method of each study and we concluded that the identified studies are at good quality to be used in any systematic review. The summary of the results that were identified as a result of using JBI tool are represented in table 1.

Table 2: The result of assessment the identified studies using JBI critical appraisal tool.

Study	Is it clear in the study what is the cause and what is the effect'?	Was there a control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete?	Do the comparisons measured in the same way?	Were the participants included in any comparisons similar?	Was appropriate statistical analysis used?	Were outcomes measured in a reliable way?
(Huang et al., 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
(Erfani Majd N et all., 2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
(K.I et al., 2018)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
(Agnes Jenitha and Kanimozhi, 2016)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes

The characteristics of the collected Studies.

As a result of deep search in different databases four studies were selected according to the JBI critical appraisal tool, the inclusion and exclusion criteria and deep reviewing of the Methodology, statistical analysis and ethical conduct. These studies examined the antidiabetic effect in AE using rates induced diabetes as model organism to explore the ability of this plant to reduce the level of blood glucose and complication of type II diabetes. All of these rates were fid and prepared for the experiments according to standard laboratory roles like institutional ethical guidelines for the care of laboratory animals of KMCH and the National Academy of Sciences. Also, the approval of the animal experiments in each study was obtained from different sources like the Animal Ethics Committee of Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz and Animal Model Experimental Ethics Committee of Chung-Shan Medical University. Finally, all the studies were reviewed according to "ARRVIE guideline for reporting animal studies". Table 2 summarizes the enrolled studies according to ARRIVE guidelines.

Table 2: Summary of studies that examined the antidiabetic effects in Abelmoschus Esculentus According to ARRIVE guidelines.

Study	Sample size	Year	Design	Randomization	Animal under investigation	Control type
(Huang et al., 2017)	8	2017	Experimental study	Simple randomization	Sprague- Dawley	Standard control
(Erfani Majd N et all., 2018)	15	2018	Experimental study	Simple randomization	Wistar albino rats	Standard control
(K.I et al., 2018)	30	2017	Experimental study	Simple randomization	Alloxan-induced Diabetic Rats	Standard control
(Agnes Jenitha and Kanimozhi, 2016)	16	2016	Experimental study	Simple randomization	Wistar Albino rates	Standard control

Phytochemical components of A. esculentus

Most of the identified studies tried to explore the phytochemical components of A. esculentus to decide its ability to become a valuable plant in the type II diabetes treatment. Various types of antioxidants, proteins and carbohydrates were found in this plant. Agnes Jenitha and Kanimozhi, 2016 reported strong evidences which can make A. esculentus a medically important plant. In their study A. esculentus was reported to have many anti-inflammatories, antioxidants, anticancer, antiulcer, antihyperlipidemic and antifungal agents which include Flavonoids, Steroids and Resins. Another important finding was found by Huang et al., 2017 who extracted many phytochemical components from A. esculentus like uronic acids, glucose, galactose, glucosamine, glucoside, pentacyclic triterpene ster. Finally, Erfani Majd N et all., 2018 concluded that total amount of phenolic and flavonoid compounds in the A. esculentus extract was 147 mg quercetin/g of dry extract and 141 mg gallic acid/g of dry extract. Summary of the phytochemical components which are identified in collected studies is shown in Table 2.

Table 2: Summary of the phytochemical components of A. esculentus in the identified studies.

S. No	Name of some phytochemical components which present in Okra
1	Flavonoids
2	Steroids
3	Resins
4	Carbohydrate
5	Quinine
6	proteins
7	gallic acid
8	Saponins
9	Coumarins
10	Glycosides

Effect of A. esculentus in Serum glucose level

All four studies reported the effect of Abelmoschus Esculentus in lowering the blood glucose by monitoring its level using different types of methods. Generally, all studies provide conclusive evidence that Abelmoschus Esculentus has the ability to lower the blood glucose level in type 2 diabetes rates. Huang et al., 2017 has conclusively found a reduction in serum glucose level in type 2 diabetic rates after four weeks of treatments with AE subfraction. The level of the blood glucose of diabetic rates in their study was 442.83±44.71 mg/dL before the treatment and started to decrease up to 209.33±46.05 mg/dL at the end of their experiment. Erfani Majd N et all., 2018 confirmed this finding by reporting a significant reduction in blood glucose level in diabetic rats after 30 days since the A. esculentus up to 210 mg/dL compared to the bingeing of the treatment 330 mg/dL. Detailed examination of the antidiabetic activity in Abelmoschus Esculentus by Agnes Jenitha and Kanimozhi, 2016 showed a conclusive reduction in the level of serum glucose in A. esculentus treated rates compared to the control group. Furthermore, K.I et al., 2018 investigated the effect using Wistar Albino rats and they found a reduction in the level of blood glucose towards normal in these types of rates. Finally, all studies confirmed that A. esculentus has the ability to reduce the level of blood glucose up to 10% (75 mg/dl) compared to the control group. Summary of the glucose level at the end of each experiment in each study compared to normal diabetic rats is shown in table 3.

Table 3: Summary of the glucose level at the end of each experiment in each study compared to normal diabetic rates.

Name of the study	Control group (diabetic induced rates)	Diabetic rates treated by A. esculentus
(Huang et al., 2017)	445.25 mg/dL	209.33 mg/dL
(Erfani Majd N et all., 2018)	273 mg/dL	210 mg/dL
(Agnes Jenitha and Kanimozhi, 2016)	212.5 mg/dL	110.8 mg/dL
K.I et al., 2018)	265.9 mg/dL	85.76 mg/dL

Effect of A. esculentus on Glycated Hemoglobin Levels HbA1C

The results of identified studies revealed a significant decrease in the formation of HbA1C in the diabetic rats treated with A. esculentus. Huang et al., 2017 reported a significant decrease in level HbA1C from 8% to 6.5% in diabetes-induced rats were given A. esculentus. Moreover, K.I et al., 2018 reported a clear decrease in Glycated hemoglobin (4.78±0.17 %) in comparison with the diabetic untreated rats (11.04±0.31%). These results are also supported

by Agnes et all and Erfani Majd N et all., 2018 who documented a clear decrease in the level of HbA1C in diabetic rats were treated via A. esculentus.

Effect of A. esculentus on the serum lipid profile of diabetic rats

Lipid profile which includes TG, cholesterol, HDL, LDL, and VLDL was also affected by A. esculentus treatment. Erfani Majd N et all., 2018 reported a significant decrease in the level of TG and cholesterol in diabetic rats treated by A. esculentus compared to non-treated diabetic rates. This result is supported by Huang et al., 2017 who concluded that A. esculentus can lower the level of TG and cholesterol in Sprague- Dawley treated by A. esculentus and they suggested that this plant possess an effective ability to improve dyslipidemia in diabetic rats. Furthermore, K.I et al., 2018 confirmed this reduction after inducing A. esculentus treatment.

Effects of A. esculentus on diabetic rats' body weight

All diabetic rates which were included in the four studies were much fatter before the treatment with A. esculentus. However, their weight gradually decreased after the treatment until the end of the studies. Sprague- Dawley -induced diabetic rats which were used by Huang et al., 2017 significantly recovered from overweight. This result is supported by Erfani Majd N et all., 2018 who reported a clear significant decrease in the rate's weight after starting A. esculentus.

Effect of A. esculentus on liver and kidney

Safety assessment in identified studies showed that A. esculentus has no harmful effect on liver and kidneys. Huang et al., 2017 concluded that treatment of all A. esculentus subfractions did not harm the kidneys and liver and it scientifically lowered the level of serum glutamic oxaloacetic transaminase (SGOT) to the normal in the Sprague- Dawley rates showing a potential of liver protective effects.

DISCUSSION

This study set out with the aim of assessing the ability of A. esculentus (Okra) to manage and control type II diabetes and its related complications through searching in different databases to find out proper studies and scientific information that examine this feature. As mentioned in the result of this systematic review A. esculentus can play an important role in treatment and prevention the type II diabetes in rates. This ability due to the presence of various antioxidants like Myricetin, Kaempferol, Oleanolic acid and Beta Sistostenol. Myricetin has

been well studied and was found to be successful in lowering blood glucose due to its antioxidant effect. According to Prabhune, Sharma and Ojha, 2017 Myricetin can decrease the adsorption of blood glucose and cholesterol from the diet. Furthermore, it can enhance glucose utilization and improve carbohydrate metabolism (Kandasamy N, 2017). Moreover, it has been shown through examination survey on habitual food consumption done by Finnish Mobile Clinic Health on random sample included 10,054 participants that Type II diabetes can be controlled by high intake of dietary myricetin (J.M. Barbosa-Filho, 2005). Another study included 42 diabetic patients received Blueberin supplement with 50 mg of myricetin reported a decrease in the level of blood glucose in those patients compared to the control group (Abidov et al., 2006). It was reported that myricetin can improve hyperglycemia through enhancing glucose uptake and glucagon synthesis by the liver of rates (I.M. Liu et all., 2005).

Another important antioxidant found in A. esculentus which is known to have an anti-glycemic effect is Kaempferol (Prabhune, Sharma and Ojha, 2017). According to Zang Y et all., 2015 kaempferol treatment can lower the level of fasting blood glucose and HbA1C in mice. In addition to this, it can lower adipose tissue accumulation and improve hyperlipidemia (Zang Y et all., 2015). Another important finding was related to the A. esculentus polysaccharide. polysaccharides and carbohydrate are proved to treat hyperglycemia and insulin resistance. According to Zhou J et all 2017 polysaccharide can be an option for type II diabetes because it can improve hyperlipidemia, hyperglycemia and oxidative stress in mice (Huang et al., 2017). It is interesting to note that Huang et al., 2017 isolated myoinositol and rhamnose from Okra which are revealed to have anti-diabetic effect in a clinical trial done by Ravelojaona V et all., 2006. Commonly, type II diabetes is associated with obesity due to an imbalance in energy usage that results from insulin resistant (Huang et al., 2017). This fact is clearly shown in the current study which found that diabetic rates lost their weight after inducing okra treatment.

From the results of systemic review, it has been shown that Okra is an excellent source of nutrients. It contains Quinine, Steroids Resins, Carbohydrate and Flavonoids. Flavonoids are powerful antioxidants with immune system and anti-inflammatory benefits. According to Hertog, 1995 consumption of flavonoid is strongly associated with longevity. In addition to this, they decrease level of hormone called leptin which affect food consumption and obesity

(Szalay, 2015). Moreover, a study published in 2013 revealed that consumption of flavonoid can improve vascular function (Szalay, 2015).

Elevation of HbA1C in non-treated diabetic rates which was observed in identified studies may due to continues hyperglycemia which lead to increase the level of glucose in the blood and thus formation glycated haemoglobin and its reduction in treated rates clearly prove the anti-hyperglycemic effect of Okra (Rohlfing et al., 2000).

It is important to note that the current study revealed improvement in triglyceride (TG) and Total Cholesterol (TC) in the rats treated with A. esculentus compared to control diabetic rates. various mechanism can explain this improvement. Erfani Majd N et all., 2018 reported that inducing Okra can reduce gene expression of SREBP1c and FAS which can finally lead to reduce the level of TG and TC. In addition to this, Okra is rich with fibers which can bind to bile acid and lower the level of total cholesterol through disturbances the bile acid reabsorption (Erfani Majd N et all., 2018).

CONCLUSION

From the results of this systematic review, it has been shown that Abelmoschus esculentus (Okra) can be considered as a valuable vegetable due to its beneficial phytochemicals. All the included studies confirmed the anti-diabetic effect of okra on type II diabetic rats. However, there are insufficient evidences to confirm its effect on human. So, Further research needs to examine more closely the links between Okra and type II diabetes in human to provide a clear view to the medical field.

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