# Journal of Applied Sciences

ISSN 1812-5654

science alert

ANSInet
an open access publisher
http://ansinet.com

OPEN ACCESS Journal of Applied Sciences

ISSN 1812-5654
DOI: 10.3923/jas.2019.585.592

# Research Article
# Dipeptidyl Peptidase IV and α-glucosidase Inhibitory Activity of *Ceratotheca sesamoides*, *Corchorus fascicularis*, *Corchorus olitorius* and *Abelmoschus esculentus*

[1]Pamhidzai Dzomba and [2]Estele Mwanza

[1]Department of Chemistry, Faculty of Science, Bindura University of Science Education, P. Bag 1020, Bindura, Zimbabwe
[2]Department of Health Sciences, Faculty of Science, Bindura University of Science Education, P. Bag 1020, Bindura, Zimbabwe

## Abstract

**Background and Objective:** *Ceratotheca sesamoides, Corchorus fascicularis, Corchorus olitorius* and *Abelmoschus esculentus* are edible bush okras used to manage *diabetes mellitus* type 2 in traditional practices worldwide. In this study we investigate the alpha-glucosidase and dipeptidyl peptidase inhibitory activity of the four bush okras' leaf, seeds and pods extracts. **Materials and Methods:** Liquid-liquid extraction was used for extracting the active phytochemicals. The extracts and standard inhibitors, sitagliptin and precose were then used in *in vitro* studies to determine percentage inhibition and $IC_{50}$ values using UV-VIS spectrophotometry. **Results:** The *C. sesamoides, C. fascicularis*, *C. olitorius* and *A. esculentus* ethanolic extracts showed significant dipeptidyl peptidase inhibitory activity with $IC_{50}$ values ranging from 1.53-92.32 μg $mL^{-1}$ and α-glucosidase inhibitory activity with $IC_{50}$ values ranging from 1.85-8.43 μg $mL^{-1}$. Most of the extracts showed greater than 50% inhibition at concentration lower than 10 μg $mL^{-1}$. Leaf and seed extracts showed the best results with $IC_{50}$ values lower than those of standard inhibitors, 2.32 and 2.38 μg $mL^{-1}$ for sitagliptin and precose, respectively. Among the okras *A. esculentus* showed the best results, $IC_{50}$ values<2 μg $mL^{-1}$. **Conclusion:** Results of the present studies show that administration of polar extracts i.e., aqueous infusions of *C. sesamoides*, *C. fascicularis*, *C. olitorius* and *A. esculentus* inhibits the enzymes, α-glucosidase and dipeptidyl peptidase. Thus the study supports the global use of the edible okra species in traditional medicine to manage diabetes mellitus type 2.

Key words: *Ceratotheca sesamoides*, *Corchorus fascicularis*, *Corchorus olitorius*, *Abelmoschus esculentus*, diabetes mellitus type 2

Received: January 12, 2019 Accepted: March 27, 2019 Published: May 15, 2019

Citation: Pamhidzai Dzomba and Estele Mwanza, 2019. Dipeptidyl peptidase iv and α-glucosidase inhibitory activity of *Ceratotheca sesamoides*, *Corchorus fascicularis*, *Corchorus olitorius* and *Abelmoschus esculentus*. J. Applied Sci., 19: 586-592.

Corresponding Author: Pamhidzai Dzomba, Department of Chemistry, Faculty of Science, Bindura University of Science Education, P. Bag 1020, Bindura, Zimbabwe Tel: +263773474525



Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Diabetes mellitus type 2 (DM T2) is the fastest growing metabolic disease worldwide characterised by insulin resistance, progressive decline in the pancreatic beta cell activity and increasing hyperglycaemia[1,2]. DM T2 is now the world's fifty leading cause of human morbidity and mortality. According to International Diabetes Federation, people suffering from DM T2 are expected to continue to rise from[3,4] 366 million in 2011-552 million 2030. Unmanaged DM T2 results in a multiple disorders including microvascular (renal and retinal) and macro-vascular (coronary, peripheral vascular and neuropathic) which are long term complications[5]. Thus better control of glycaemia lessens the development of angiopathic complications. Treatment to attain normoglycaemia is focused on increasing insulin secretion, responsive or both and decreasing the rate of metabolizing carbohydrates and fats.

Clinically accepted oral medicines for DM T2 include biguanides, sulphonylureas, meglitinides, thiazolidinediones, α-glucosidase inhibitors and dipeptidyl peptidase IV inhibitors[6,7]. Biguanides, the widely prescribed drugs act by blocking the production of glucose in the liver and sometimes stimulate uptake of glucose by tissue[7]. They increase the binding effect of insulin on receptors thus reduce insulin resistance however these do not stimulate the secretion of insulin by the pancreas[8]. Although biguanides can reduce glycated haemoglobin by 1-2, only 25% of patients may be controlled adequately by monotherapic administration[9]. Adverse effects including abdominal pain, blotting, nausea, diarrhoea and anorexia limits its use in controlling DM T2. It is no-longer prescribed to patients with renal insufficiency, liver challenges and metabolic acidosis[9]. Sulphonylureas and meglitinides are known as insulin secretagogues that is they cause the pancreas to secrete insulin. Although these drugs are effective in reducing glycated haemoglobin, many patients may experience loss of drug effect after years of successful treatment due to progressive failure of beta cells. In such a case combination therapy is recommended. Thus in future many patients will require multiple therapies[10]. Sulphonylureas and meglitinides also have a risk of weight gain. Thiazolidinediones function by regulating carbohydrate and lipid metabolism. They enhance insulin action but have no effect on its secretion[8]. Major draw backs of thiazolidinediones include fluid retention, unpredicted weight gain, development of peripheral oedema and mild anaemia [9]. Alpha-glucosidase and dipeptidyl peptidase inhibitors function by inhibiting enzymes. These are well tolerated and have fewer adverse effects thus current studies are now focusing on searching for food based alternative remedies which have similar mode of action. Synthetic and botanical inhibitors of alpha-glucosidase and dipeptidyl peptidase have been reported in previous studies however clinical application has been hampered by lack of potency *in vivo* due to lack of oral bio-availability, poor permeability in membranes and weak selectivity[11]. It is crucial due to the above arguments that the search for new anti-DM T2 remedies continues.

Bush okras including, *Abelmoschus esculentus*, *Ceratotheca sesamoides*, *Corchorus olitorius* and *Corchorus fascicularis*, Fig. 1 are widely consumed in Africa, Asia and some parts of Europe as vegetables[12]. *A. esculentus*, *C. sesamoides, C. olitorius* and *C. fascicularis* are used to manage DM T2 in traditional practices however scientific studies to support this use is still limited. Thus the present study was designed to investigate dipeptidyl peptidase IV and alpha glucosidase inhibitory activity of four bush okra species, *A. esculentus*, *C. sesamoides, C. olitorius* and *C. fascicularis.*

The *C. olitorius* and *C. fascicularis* consist of several types of phytocompounds including phytosterols, triterpenoids and polyphenolic compounds which have portrayed anti-inflammatory, anti-cancer, anti-histaminic, anti-oestrogenic and antipyretic activity[13,14].

## MATERIALS AND METHODS

**Plant material collection:** Plant material were collected during the rainy season (January-April) from Mashonaland East in Mudzi district and Mashonaland Central in Bindura district with the help of elderly persons and separated into pods, seeds and leaves. Samples were kept in a freezer until required for analysis. The plants were further authenticated by taxonomists at the Harare National Herbarium and voucher specimens 2017/1, 2, 3, 4 were kept in the Bindura University of Science Education natural product herbal library for future reference.

**Sample preparation:** Fresh plant material, 60 g each was crushed into a paste using a wooden mortar and pestle and extracted three times with 100 mL of absolute ethanol. The filtrate were then combined and the solvent evaporated on a Buchi rotary evaporator to dryness. The contents were weighed and dissolved in 9:1 water-ethanol solution to a final volume of 10 mL. The resultant stock solutions were then kept in a refrigerator waiting further analysis.


Fig. 1: Pictorial view of *Ceratotheca sesamoides*, *Corchorus fascicularis*, *Corchorus olitorius* and *Abelmoschus esculentus*

**Dipeptidyl peptidase IV inhibition assay:** Pods, Leaves and seeds extracts DPPIV inhibitory activity was screened following a method reported by Bharti *et al.*[15] with minor modifications using a total well volume of 100 Ml. Crude extracts or sitagliptin (standard inhibitor of DPPIV) were diluted to various concentration in the range 0-100 μg $mL^{-1}$ using 50 mM TrisHCl buffer at pH7.5 to a final volume of 35 μL. Absorbance of the solutions were recorded at 405 nm followed by adding 15 μL of 0.05 U $mL^{-1}$ of DPPIV enzyme. One unit of enzyme was taken as the amount of an enzyme required to catalyze the production of 1 μM of paranitroanilidine per minute. The mixture was pre-incubated for 10 min at 37°C to allow maximum contact of enzyme with inhibitor followed by addition of 50 μL of 0.2 mM Glypro-p-nitroanilidine diluted in TrisHCl buffer. The resultant mixture was incubated at 37°C for 30 min. The reaction was terminated by adding 25 μL of 25% glacial acetic acid. The absorbance results were compared with results of a control experiment (without inhibitor). The percentage inhibition was computed using the equation:

$$I\,(\%) = \frac{A_C - A_S}{A_C}$$

where, I (%) is percentage inhibition, $A_C$: Absorbance of control experiment (without inhibitor) and $A_S$: Is absorbance of experiment with standard inhibitor or with extracts.

The $IC_{50}$ value was defined as the concentration of extract that inhibited 50% of DPPIV activity under the assay conditions dose-activity curve.

**Alpha-glucosidase inhibition assay:** The assay was conducted following a method reported by Sabitha *et al.*[16].

**Statistical analysis:** The results are expressed as means±standard error of three replicate analysis. Differences between the group means was analyzed using the IBM SPSS version 20 software by applying a one way ANOVA with the Turkey-karner *post hoc* test to identify significance among groups. A $p<0.05$ was considered to be statistically significant.

## RESULTS

**Dipeptidyl peptidase IV inhibition activity:** Results in Fig. 2 show that *C. sesamoides*, *C. olitorius*, *C. fascicularis* and *A. esculentus* extracts are natural inhibitors of DPPIV with leaves and seeds showing an inhibition activity that was not

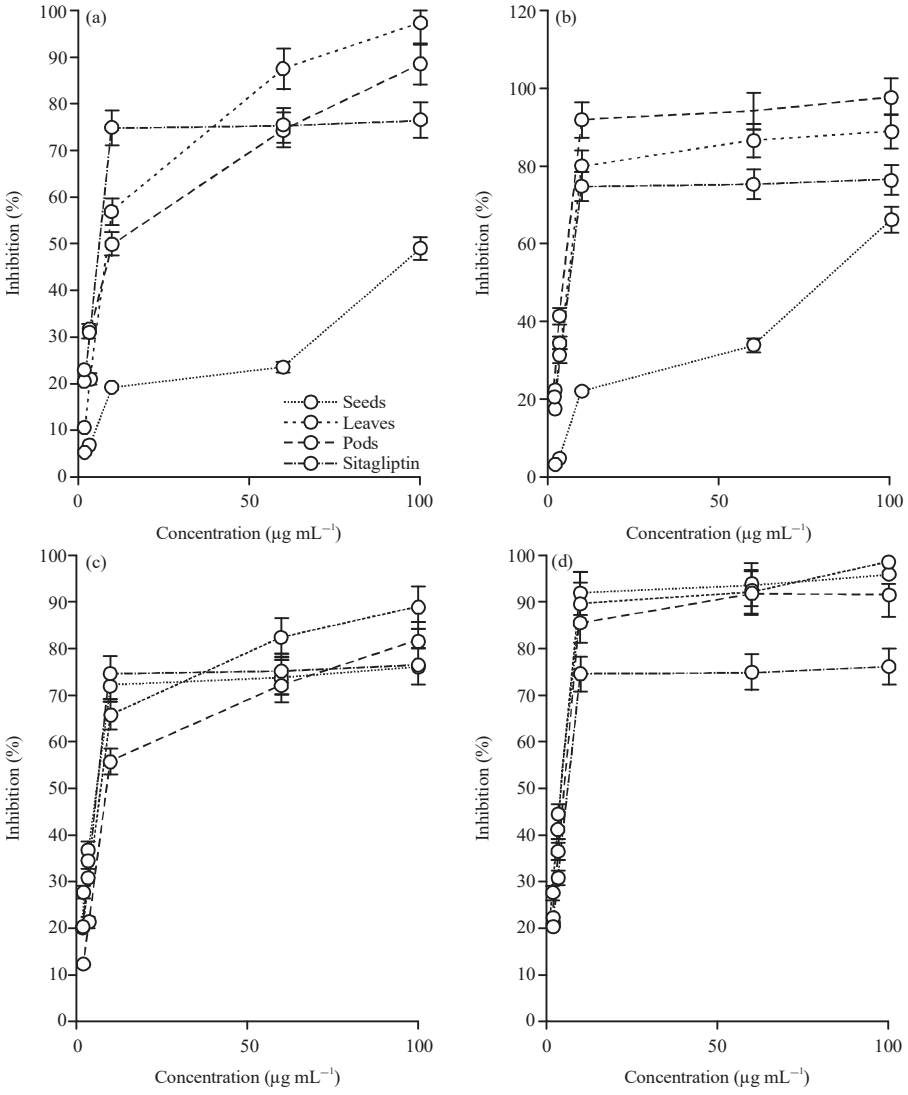


Fig. 2(a-d): Dipeptidyl peptidase IV inhibition activity of (a) *C. sesamoides*, (b) *C. fascicularis*, (c) *C. olitorius* and (d) *A. esculentus* in comparison to standard inhibitor sitagliptin

significantly different from that of the standard inhibitor sitagliptin for concentrations lower than 10 µg mL$^{-1}$, ($p>0.05$). Seeds and pods extracts from *C. sesamoides* and *C. olitorius* showed a lower inhibition activity while for *C. fascicularis* and *A. esculentus* the inhibition pattern was similar for all the extracts. As the concentration was increased from 10 µg mL$^{-1}$, the percentage inhibition activity increased slightly however the extracts from *C. fascicularis* and *A. esculentus* became better inhibitors than sitagliptin (Fig. 2b and d). For *C. sesamoides* the percentage inhibition trend was leaves, 97.1±0.06>pods, 88.4±0.03> sitagliptin, 76.4±0.01> seeds, 48.9±0.05% (Fig. 2a), while for *C. olitorius* the trend was leaves, 97.6±0.09>seeds, 88.9±0.00> sitagliptin, 76.4±0.00>pods 66.2±0.03%, (Fig. 2b). For *C. olitorius* (Fig. 2c), the percentage inhibition trend was leaves, 88.9±0.05>pods, 81.6±0.07>sitagliptin, 76.4±0.02 = seeds, 76.4±0.03%, (Fig. 2c) and lastly that for *A. esculentus,* (Fig. 2d) was leaves, 98.9±0.00>pods, 96.2±0.09>seeds, 91.6±0.03> sitagliptin, 76.4±0.03. Thus all the extracts from *A. esculentus* showed higher inhibition than sitagliptin a tight binder inhibitor for DPPIV.

Table 1 shows $IC_{50}$ values for the inhibition of DPPIV. The $IC_{50}$ values ranged from 1.53-92.32 µg mL$^{-1}$. The *A. esculentus* extracts showed the greatest inhibition activity with $IC_{50}$ values, 1.53, 1.55 and 1.58 µg mL$^{-1}$ and all are significantly lower than for sitagliptin, 2 .32 µg mL$^{-1}$ ($p<0.05$). Also *C. fascicularis* leaf and seeds extract showed greater inhibition activity than sitagliptin $p<0.05$. The *C. sesamoides*

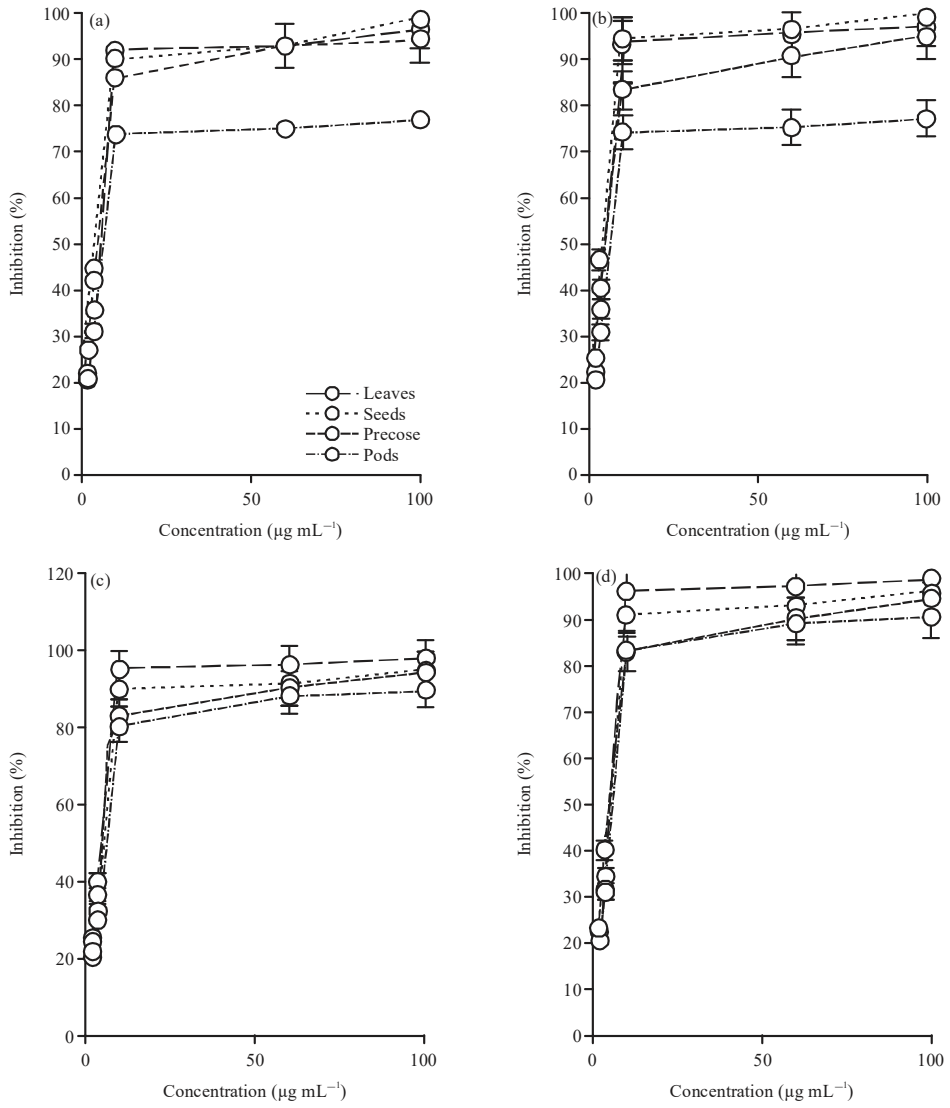


Fig. 3(a-d): A-glucosidase inhibition activity of (a) *C. sesamoides*, (b) *C. fascicularis* (c) *C. olitorius* and (d) *A. esculentus* in comparison to standard inhibitor precose

Table 1: Half maximal inhibitory concentration ($IC_{50}$) of *C. sesamoides*, *C. fascicularis*, *C. olitorius, A. esculentus* and standard inhibitor sitagliptin

| Species | Part | $IC_{50}$ values (µg mL$^{-1}$) |
|---|---|---|
| *C. sesamoides* | Seeds | 92.32 |
| | Leaves | 2.33 |
| | Pods | 2.62 |
| *C. fascicularis* | Seeds | 1.81 |
| | Leaves | 1.78 |
| | Pods | 72.40 |
| *C. olitorius* | Seeds | 2.25 |
| | Leaves | 2.31 |
| | Pods | 18.22 |
| *A. esculentus* | Seeds | 1.53 |
| | Leaves | 1.55 |
| | Pods | 1.58 |
| Standard inhibitor sitagliptin | - | 2.32 |

(leaf extract) and *C. olitorius* (seeds and leaf extract) showed inhibition activity that was significantly similar to that of sitagliptin, ($p>0.05$).

**Alpha-glucosidase inhibition assay:** Figure 3 shows that *C. sesamoides*, *C. fascicularis*, *C. olitorius* and *A. esculentus* extracts inhibit α-glucosidase in a similar pattern as the commercial drug precose. A sharp increase in percentage inhibition activity was observed within the 0-10 µg mL$^{-1}$ concentration range. Later on the inhibition activity increased steadily. The percentage inhibition activity of the extracts and the standard inhibitor precose did not differ significantly for all the bush okra species within the 0-10 µg mL$^{-1}$ concentration

Table 2: Half maximal inhibitory concentration ($IC_{50}$) of *C. sesamoides*, *C. fascicularis*, *C. olitorius*, *A. esculentus* and standard inhibitor precose on α-glucosidase

| Species | Part | $IC_{50}$ values (μg $mL^{-1}$) |
|---|---|---|
| *C. sesamoides* | Seeds | 2.24 |
| | Leaves | 2.12 |
| | Pods | 5.22 |
| *C. fascicularis* | Seeds | 2.12 |
| | Leaves | 2.06 |
| | Pods | 7.43 |
| *C. olitorius* | Seeds | 2.25 |
| | Leaves | 2.16 |
| | Pods | 8.43 |
| *A. esculentus* | Seeds | 1.85 |
| | Leaves | 2.05 |
| | Pods | 2.10 |
| Standard inhibitor precose | - | 2.38 |

range, ($p>0.05$). Above 10 μg $mL^{-1}$, extracts from *C. sesamoides* and *C. fascicularis* pods showed inferior inhibition activity than precose, seed and leaf extracts (Fig. 3a and b). The *C. fascicularis* seeds and leaf extracts showed significantly greater inhibition activity than precose $p<0.05$ (Fig. 3b). The case was also similar for *C. olitorius* and *A. esculentus* leaf and seeds extracts (Fig. 3c and d). When the concentration was increased to 100 μg $mL^{-1}$ the inhibition activity of the extracts and precose did not differ significantly $p>0.05$ showing that concentration of the inhibitor ceased to affect the rate of catalysis.

Table 2 shows that all the extracts from *A. esculentus*, $IC_{50}$ values, 1.85, 2.05 and 2.10 μg $mL^{-1}$ for seeds, leaves and pods, respectively are better α-glucosidase inhibitors than precose with an $IC_{50}$ value of 2.38 μg $mL^{-1}$. Also leaf and seed extracts of *C. sesamoides*, *C. fascicularis* and *C. olitorius* are better α-glucosidase inhibitors than precose $IC_{50}$ values<2.38 μg $mL^{-1}$. The results clearly showed that *A. esculentus* seed extracts are the best inhibitors of α-glucosidase. Precose is a better inhibitor than extracts from *C. sesamoides*, *C. fascicularis* and *C. olitorius* pods, $IC_{50}$ values>2.38 μg $mL^{-1}$.

## DISCUSSION

The four bush okras, *C. sesamoides, C. olitorius*, *C. fascicularis* and *A. esculentus* extracts portrayed potent inhibitory activity against DPPIV that was comparable to that of the standard inhibitor sitagliptin. Previous studies have shown that inhibition of DPPIV provides a novel approach for treatment of DM T2[17,18]. The DPPIV is responsible for the inactivation of glucagon like peptide that has the role of stimulating insulin secretion and the increase in the population of beta cells[15,19]. Sitagliptin is sold under the name januvia in the market. It is an oral medicine that can be used in combination with metformin[9]. Thus the four bush okras can be potent DM T2 alternative medicine to sitagliptin which has revealed side effects in some patients. The side effects in some patients include pancreatitis, frequent urination and weight gain[9]. Among the four okras, *A. esculentus* is the best substitute with $IC_{50}$ values for both seed, leaf and pods extract lower than that for sitagliptin. Comparing the extracts from seed, leaf and pods the seed extract is a superior alternative inhibitor. The *A. esculentus* is consumed as a vegetable worldwide[20]. It can be used in salads, soups and stews. It is more a diet than staple food. The *A. esculentus* seeds consist of oligomeric catechin, flavonols derivatives, hydroxycinnamic derivatives and quercetin[20]. Previously these phytochemicals have been reported to consist of DPPIV inhibitory activity[21,22].

The *C. sesamoides*, *C. fascicularis*, *C. olitorius* seed and leaf extracts are also better potent DPPIV inhibitors than sitagliptin, $IC_{50}$ values< that of sitagliptin. According to Khan *et al.*[13], *C. fascicularis* and *C. olitorius* consisted of tetraterpenes (ursolic acid, corosolic acid and betulinic acid), flavonoids (quercetin, kaempferol and flavonoids) and phenolic acids (scopolin and chlorogenic acid). In a related study[23] anti-diabetic activity of the tetraterpene, betulinic acid was demonstrated using protein tyrosine phosphatase 1b inhibition. Quang *et al.*[24] also demonstrated the anti-diabetic activity of flavonoids and prenylated xanthones using the same assay. Lacroix and Li-Chan[25] demonstrated whey protein isolate can be potential sources for sources of DPP-IV and α-glucosidase inhibitors with an $IC_{50}$ value of 0.036 mg $mL^{-1}$.

The percentage inhibition activity and $IC_{50}$ values showed that *C. sesamoides, C. olitorius, C. fascicularis* and *A. esculentus* extracts are good inhibitors of α-glucosidase with an activity that was better or comparable to that of the standard drug precose. Precose chemically known as o-4, 6-dideoxy-4-[(1S,4R, 5S,6S)-4, 5, 6-tryhydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl]amino] α-D-glucopyranosyl-(1, 2, 3, 4)-o-α-D-glucopyranosyl-(1, 2, 3, 4)-D-glucose is an oligosaccharide prescribed as an oral α-glucosidase competitive inhibitor for use as a drug for DM[1] T2. The biggest challenge with precose is that there is no fixed dosage thus it has to be individualized according to effectiveness and tolerance[8]. Common side effects of precose among some patients include, constipation, rectal bleeding, stomach pain, diarrhea and pneumatosis cystoides[1]. Thus the present results are interesting. They showed that *C. sesamoides*,

*C. olitorius, C. fascicularis* and *A. esculentus* can also be used as alternative remedies to precose especially to patients showing serious side effects when prescribed precose. Among the okras once again *A. esculentus* proved to be the best alternative followed by *C. fascicularis* then *C. sesamoides* and lastly *C. olitorius* see (Table 2). While all extracts from *A. esculentus* showed better activity than precose only leaf and seeds extracts of *C. sesamoides, C. olitorius, C. fascicularis* portrayed superior activity than precose. The $IC_{50}$ values obtained in the present study are comparable to values reported by Li *et al.*[26] for *Punica granatum* flower extract and Zhang *et al.*[27] for *Castanea mollissima* extracts. $IC_{50}$ values around 1.8 and 0.33 μg $mL^{-1}$, respectively. However the values are lower than values reported by Sabitha *et al.*[16]. The lower $IC_{50}$ values show that the extracts bind to the enzyme with higher affinity than the substrate and the standard inhibitor precose. This may be due to the fact that the extracts consist of a mixture of compounds that may bind either at the active site or the allosteric site or to metals responsible for the maintenance of the quaternary structure of the enzyme.

## CONCLUSION

The experimental evidence of the present study support the use of *C. sesamoides, C. olitorius, C. fascicularis* and *A. esculentus* in management of DM T2 in traditional medicine. The ethanolic extracts show significantly better or similar inhibition activity for both DPPIV and α-glucosidase as compared to standard inhibitors sitagliptin and precose respectively. Among the extracts the seed and leaf extracts showed the best results as compared to pods extracts. For *A. esculentus,* all the extracts showed better results than the standards showing that *A. esculentus* is the best candidate than the other okra species. Since the anti-diabetic drugs sitagliptin and precose have side effects on some patients, *C. sesamoides, C. olitorius, C. fascicularis* and *A. esculentus* can be alternative remedies. The okra species can also be future candidates for developing food derived DPPIV and α-glucosidase inhibitors as potential approach for glycaemia regulation.

## SIGNIFICANCE STATEMENT

This study discovered that *Ceratotheca sesamoides, Corchorus fascicularis, Corchorus olitorius* and *Abelmoschus esculentus* extracts inhibits α-glucosidase and dipeptidyl peptidase 1V thus providing a scientific explanation for the use of the four bush okra species in the management of diabetes in traditional medicine. The results shows that the four okra species are good candidates for developing food based remedies for diabetes type 2.

## ACKNOWLEDGMENT

The authors would like to appreciate the post graduate and research center of Bindura University of science education for block grant allocation 2017 to purchase standards and other laboratory reagents for this study. Acknowledgments are also given to diabetic patients who provided useful information on the use of the okra species in management of DM T2. The information you gave us provided the impetus for this study.

## REFERENCES

1. Whittaker, C., 2010. A review of oral diabetic. S. A. Pharm. J., 10: 20-25.
2. Nyenwe, E.A., T.W. Jerkins, G.E. Umpierrez and A.E. Kitabchi, 2011. Management of type 2 diabetes: Evolving strategies for the treatment of patients with type 2 diabetes. Metabolism, 60: 1-23.
3. Wild, S., G. Roglic, A. Green, R. Sicree and H. King, 2004. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care, 27: 1047-1053.
4. Riyanti, S., A.G. Suganda and E.Y. Sukandar, 2016. Dipeptidyl peptidase-iv inhibitory activity of some Indonesian medicinal plants. Asian J. Pharm. Clin. Res., 9: 375-377.
5. Walker, R. and C. Edwards, 2003. Clinical Pharmacy and Therapeutics. 3rd Edn., Churchill Livingstone, London, ISBN: 9780443071386, pp: 37-42.
6. Bosenberg, L.H. and D.G. van Zyl, 2008. The mechanism of action of oral antidiabetic drugs: A review of recent literature. J. Endocrinol. Metab. Diabetes South Afr., 4: 80-88.
7. Todd, J.F. and S.R. Bloom, 2007. Incretins and other peptides in the treatment of diabetes. Diabet. Med., 24: 223-232.
8. Rakel, R.E., 2007. Textbook of Family Medicine. 7th Edn., Saunders/Elsevier, Philadelphia, ISBN: 9781416024675, pp: 1405-1604.
9. Cecil, R.L.F., 2008. Cecil Medicine. 23rd Edn., Saunders Elsevier, Philadelphia, ISBN: 9781416044789, pp: 126-132.
10. Gerich, J.E., 2001. Matching treatment to pathophysiology in type 2 diabetes. Clin. Ther., 23: 646-659.
11. Cragg, G.M., P.G. Grothaus and D.J. Newman, 2009. Impact of natural products on developing new anti-cancer agents-A review. Chem. Rev., 109: 3012-3043.
12. Adetuyi, F.O. and T.A. Ibrahim, 2014. Effect of fermentation time on the phenolic, flavonoid and vitamin C contents and antioxidant activities of Okra (*Abelmoschus esculentus*) seeds. Nig. Food J., 32: 128-137.

13. Khan, M.S.Y., S. Bano, K. Javed and M.A. Mueed, 2006. A comprehensive review on the chemistry and pharmacology of *Corchorus* species-A source of cardiac glycoside,s, triterpenoids, ionones, flavonoids, coumarins, steroids and some another compounds. J. Sci. Ind. Res., 65: 283-298.
14. Rajput, A.P. and T.A. Rajput, 2012. Isolation of two phenolic compounds from ethanol extract of leaves of *Corchorus fascicularis* Lam. Biotechnology, 11: 292-295.
15. Bharti, S.K., S. Krishnan, A. Kumar, K.K. Rajak, K. Murari, B.K. Bharti and A.K. Gupta, 2012. Antihyperglycemic activity with DPP-IV inhibition of alkaloids from seed extract of *Castanospermum australe*: Investigation by experimental validation and molecular docking. Phytomedicine, 20: 24-31.
16. Sabitha, V., K. Panneerselvam and S. Ramachandran, 2012. *In vitro* α-glucosidase and α-amylase enzyme inhibitory effects in aqueous extracts of *Abelmoscus esculentus* (L.) Moench. Asian Pac. J. Trop. Biomed., 2: S162-S164.
17. Tatosian, D.A., Y. Guo, A.K. Schaeffer, N. Gaibu and S. Popa *et al*., 2013. Dipeptidyl peptidase-4 inhibition in patients with type 2 diabetes treated with saxagliptin, sitagliptin or vildagliptin. Diabetes Ther., 4: 431-442.
18. Tsurutani, Y., M. Omura, Y. Matsuzawa, J. Saito and M. Higa *et al*., 2017. Efficacy and safety of the dipeptidyl Peptidase-4 inhibitor Sitagliptin on atherosclerosis, β-cell function and glycemic control in Japanese patients with type 2 diabetes mellitus who are treatment Naïve or poorly responsive to Antidiabetes agents: A multicenter, prospective observational, uncontrolled study. Curr. Ther. Res., 84: 26-31.
19. Yogisha, S. and K.A. Raveesha, 2010. Dipeptidyl peptidase IV inhibitory activity of *Mangifera indica*. J. Nat. Prod., 3: 76-79.
20. Gemede, H.F., N. Ratta, G.D. Haki, A.Z. Woldegiorgis and F. Beyene, 2015. Nutritional quality and health benefits of Okra (*Abelmoschus esculentus*): A review. J. Food Process Technol., Vol. 6. 10.4172/2157-7110.1000458.
21. Fan, J., M.H. Johnson, M.A. Lila, G. Yousef and E.G. de Mejia, 2013. Berry and citrus phenolic compounds inhibit dipeptidyl peptidase IV: Implications in diabetes management. Evid.-Based Complement. Altern. Med., Vol. 2013. 10.1155/2013/479505.
22. Lacroix, I.M.E. and E.C.Y. Li-Chan, 2016. Food-derived dipeptidyl-peptidase IV inhibitors as a potential approach for glycemic regulation-current knowledge and future research considerations. Trends Food Sci. Technol., 54: 1-16.
23. Shah, R.M., Ishtiaq, S.M. Hizbullah, S. Habtemariam and A. Zarrelli *et al*., 2016. Protein tyrosine phosphatase 1B inhibitors isolated from *Artemisia roxburghiana*. J. Enzyme Inhib. Med. Chem., 31: 563-567.
24. Quang, T.H., N.T.T. Ngan, C.S. Yoon, K.H. Cho and D.G. Kang *et al*., 2015. Protein tyrosine phosphatase 1B inhibitors from the roots of *Cudrania tricuspidata*. Molecules, 20: 11173-11183.
25. Lacroix, I.M.E. and E.C.Y. Li-Chan, 2013. Inhibition of Dipeptidyl Peptidase (DPP)-IV and α-glucosidase activities by pepsin-treated whey proteins. J. Agric. Food Chem., 61: 7500-7506.
26. Li, Y., S. Wen, B.P. Kota, G. Peng, G.Q. Li, J. Yamahara and B.D. Roufogalis, 2005. *Punica granatum* flower extract, a potent α-glucosidase inhibitor, improves postprandial hyperglycemia in Zucker diabetic fatty rats. J. Ethnopharmacol., 99: 239-244.
27. Zhang, J., S. Zhao, P. Yin, L. Yan and J. Han *et al*., 2014. α-Glucosidase inhibitory activity of polyphenols from the burs of *Castanea mollissima* Blume. Molecules, 19: 8373-8386.