Research Article

In vivo inhibitory activities of husk extract and fractions of *Zea mays* on alpha amylase and alpha glucosidase

Jude E. Okokon^{1*}, Godwin Enin², Mandu E. Nyong¹, Blessing C. Anyanwu², Godswill F. Dick²

¹Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo, Uyo, Nigeria

²Department of Chemistry, Faculty of Science, University of Uyo, Uyo, Nigeria

Received: 12 November 2021

Revised: 11 December 2021

Accepted: 31 December 2021

Abstract

Objective: *Zea mays* husk is used in Ibibio traditional medicine for the treatment of various ailments including diabetes mellitus, malaria and ulcer. Aim of present study was to investigate inhibitory activities of husk extract and fractions of *Zea mays* on alpha amylase and alpha glucosidase. **Material and methods:** The husk extract (187-561 mg/kg) and fractions (n-hexane, dichloromethane, ethyl acetate and methanol, 374 mg/kg) of *Zea mays* were evaluated in rats for inhibitory effect on alpha amylase and alpha glucosidase enzymes using starch, sucrose and maltose as substrates. Acarbose was used as referenced drug. **Results:** The husk extract caused significant ($p < 0.05$) reduction in blood glucose levels of treated rats though non dose-dependently with the various substrates used. The methanol fraction followed by ethyl acetate fraction exerted the highest inhibitory effect when starch and sucrose were used as substrates, while DCM fraction was the most active fraction when maltose was used as substrate. **Conclusion:** The results suggest that the husk and fractions of *Z. Mays* have the potentials to inhibit alpha amylase and glucosidase in rats.

Keywords: *Zea mays*, hypoglycaemia, alpha amylase, alpha glucosidase

Introduction

Zea mays L. (Poaceae) commonly called maize or corn, is a grass and food plant cultivated for human and animal benefits. The plant is tall and bears ears that are enclosed in modified leaves known as husks (Simmonds, 1979). In addition to its nutritive values, various parts of the plants are used in ethnomedicine for the treatment of several ailments such as diabetes (Foster and Duke, 1990; Gill, 1992; Abo et al., 2008; Brobbey et al., 2017; Okokon et al., 2017a), cough (Gill, 1992), inflammatory diseases (Okokon et al., 2016), pains and arthritis (Owoyele et al., 2010) and ulcer (Jadhav, 2016). Reported pharmacological properties of the husk extract which include; analgesic, anti-inflammatory (Owoyele et al., 2010), antioxidant (Dong et al., 2014), antidepressant (Okokon et al., 2016), antimalarial and antiplasmodial (Okokon et al., 2017a),

hepatoprotective (Okokon et al., 2017b; Okokon et al., 2020; Udobang et al., 2019), antidiabetic and hypolipidemic (Okokon and Mandu, 2018) and nephroprotective (Okokon et al., 2017c; Okokon et al., 2019), antiulcer (Okokon et al., 2018) and antiobesity (Okokon et al., 2021) activities. The median lethal dose (LD_{50}) of the ethanol husk extract was determined to be 1874.83 mg/kg (Okokon et al., 2016). Isolated compounds from the husk extract include; arabinoxylan (Ogawa et al., 2005), phenolic compounds (gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, ferulic acid, rutin, resveratrol, and kaempferol) (Dong et al., 2014), anthocyanins (Li et al., 2008) and stigmasteryl stearate and stigmasteryl palmitate (Okokon et al., 2021). In this study, we report *in vivo* alpha amylase and alpha glucosidase inhibitory activities of the husk extract and fractions of *Zea mays*.

Materials and methods

Collection of plant materials

Fresh husks of *Zea mays* were collected in August 2020

*Address for Corresponding Author:

Jude E. Okokon

Department of Pharmacology and Toxicology, Faculty of Pharmacy,
University of Uyo, Uyo, Nigeria

E-mail: judeefiom@yahoo.com

DOI: <https://doi.org/10.31024/apj.2021.6.6.2>

2456-1436/Copyright © 2021, N.S. Memorial Scientific Research and Education Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

from Farmland in Uruan in Uruan LGA, Akwa Ibom State, Nigeria. The husks were identified and authenticated as *Zea mays* by a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium specimen (FPH, 614) was deposited at the Faculty of Pharmacy Herbarium, University of Uyo, Uyo.

Extraction

Fresh husk of *Zea mays* were washed, cut into smaller pieces and dried under shade for two weeks. The husks were further pulverized to powder using electric grinder. The powdered leaves material was divided into two parts; one part (1.5 kg) was macerated in 50% ethanol (7.5 L) for 72 hours at room temperature (28 ±2 40°C). While the other part, (1.5 kg) was successively and gradually macerated for 72 h in each of these solvents (2 x 5L), n-hexane, dichloromethane, ethyl-acetate and methanol to give corresponding fractions of these solvents. These were thereafter filtered, and the liquid filtrates were concentrated and evaporated to dryness in *vacuo* 40°C using a rotary evaporator (BuchiLab, Switzerland). The yields of extract and fractions were calculated and they were stored in a refrigerator at -4°C, until used for the proposed experiments.

Animals

Swiss albino male rats (123 – 148g) used for these experiments were gotten from Animal house of Department of Pharmacology and Toxicology, University of Uyo. The animals were housed in standard cages and were maintained on a standard pelleted feed (Guinea feed) and water *ad libitum*. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo.

In vivo alpha-Amylase inhibitory study

Fifty Wistar rats were divided into 10 groups of 5 rats each. The rats in all groups were fasted for 18 h and fasting blood glucose concentration was first taken at 0 min before administration. Group I, as the normal control, received distilled water (10 mL/kg). Group II rats were orally administered starch at 2 g/kg body weight (orally with distilled water as vehicle) and distilled water (10 mL/kg) simultaneously. Rats in group III were administered starch (2 g/kg) and the standard drug (acarbose) at 100 mg/kg simultaneously. Groups IV,V and VI were administered simultaneously, starch (2 g/kg) and *Zea mays* extract at 187, 374 and 516 mg/kg respectively while groups VII-X rats were administered starch (2 g/kg) and fractions (n-hexane, dichloromethane, ethyl acetate and methanol) at 374 mg/kg respectively. All administrations were done orally and blood glucose concentration was monitored at 30, 60, 90, 120 and 180 min (Gidado et al., 2019).

In vivo glucosidase inhibitory study

Similar procedure described above was employed for this study

with sucrose and maltose used as substrates (Gidado et al., 2019).

Blood Glucose Determination

Drops of blood from tip of rats' tails were dropped on stripes and glucose concentration was measured using a glucometer according to manufacturer's specifications (Accu-chek, Indiana). The glucometer works with the following principle; the blood sample is exposed to a membrane covering the reagent pad (strip), which is coated with an enzyme (glucose oxidase, glucose dehydrogenase). The reaction causes a colour change and the intensity of this change is directly proportional to the amount of glucose in the blood sample. Light from an LED strikes the pad surface and is reflected to a photodiode, which measures the light intensity and converts it to electrical signals. An electrode sensor measures the current produced when the enzyme converts glucose to gluconic acid. The resulting current is directly proportional to the amount of glucose in the sample (WHO, 2011).

Statistical Analysis and Data Evaluation

Data obtained from this work were analysed statistically using ANOVA (one –way) followed by a post test (Tukey-Kramer multiple comparison test). Differences between means were considered significant at 5% level of significance ie $p \leq 0.05$.

In vivo alpha amylase and glucosidase inhibition assay

Results

Administration of starch (2 g/kg) caused varying percentages of increase in blood glucose concentrations after 30 mins. The percentages were starch (63.18%), extract/fractions treated groups (1.19-29.71%) and acarbose-treated group (17.97%). These increases were reduced after 90 min with animals treated with the middle dose of the extract (374 mg/kg) and methanol fraction having 0%, ethyl acetate group (13.80%) and n-hexane group (17.87%) increase in BGL. These decreases were significant and sustained for 180 min in middle dose (374 mg/kg), methanol and ethyl acetate fractions-treated groups. However, co-administration of the starch with acarbose prominently inhibited the rise in the blood glucose concentrations (Table 1).

Administration of sucrose (2 g/kg) produced a 46.01% increase in blood glucose concentration 30 minutes post-administration of the sucrose in the control group and 33.05-87.83 % increases in blood glucose concentration of extract/fractions-treated groups. The blood glucose concentrations were significantly reduced in lower doses

Table 1. Effect of ethanol husk extract and fractions of *Zea mays* on Blood Glucose level of rat after oral administration of starch load

Treatment	Dose (mg/kg)	Blood Glucose Level Mg/Dl In Min					
		0 min	30 min	60 min	90 min	120 min	180 min
Control normal saline	-	86.00±11.53	87.66±7.12(1.93)	87.66±7.62(1.93)	73.66±6.17	91.0±7.50(5.81)	80.00±6.02
Starch		73.33±8.25	119.66±5.45 ^a (63.18)	115.66±1.33 ^a (57.72)	104.66±2.60 ^a (42.72)	95.66±3.75 ^a (30.45)	92.0±6.35(25.46)
Acarbose	100	72.33±2.69	85.33±12.97(17.97)	80.33±7.21(11.06)	76.33±3.48(5.53)	74.0±1.00(2.30)	72.33±8.68(0)
Crude extract	187	75.00±3.97	90.33±5.37 ^a (20.44)	86.00±5.90(14.66)	77.33±3.71(3.10)	80.00±6.65(6.66)	76.33±6.36(1.77)
	374	88.00±6.08	103.33±3.18 ^a (17.42)	82.0±5.68	81.66±3.38 ^a	63.66±2.40	78.66±4.05
	561	83.00±4.72	107.66±2.33 ^a (29.71)	95.66±2.33(15.25)	78.66±5.36	72.0±3.78	73.0±4.58
n-hexane fraction	374	87.66±6.98	107.0±5.01 ^a (22.81)	103.33±2.07 ^a (17.87)	89.33±8.87 ^a (1.90)	95.66±9.73(9.12)	85.66±7.21
Dichloromethane fraction	374	76.66±4.84	95.33±3.84 ^a (24.35)	98.33±5.17(28.26)	88.0±4.00 ^a (14.79)	85.33±3.48 ^a (11.30)	82.66±5.33(7.82)
Ethyl acetate fraction	374	96.66±7.26	107.0±4.16 ^a (10.69)	110.0±5.19(13.80)	94.30±6.64()	92.33±8.25()	95.33±10.33()
Methanol fraction	374	111.0±4.61	112.33±9.52 ^a (1.19)	98.66±13.29()	88.66±10.41()	102.0±2.64()	99.66±2.40()

Data is expressed as MEAN ± SEM, Significant at ^ap<0.05, when compared to control. (n=6). Values in parenthesis are percentage increase in blood glucose concentrations compared to 0 min in the same group.

Table 2. Effect of ethanol husk extract and fractions of *Zea mays* on Blood Glucose level of rat after oral administration of sucrose load

Treatment	Dose (mg/kg)	Blood Glucose Level Mg/Dl In Min					
		0 min	30 min	60 min	90 min	120 min	180 min
Control normal saline	-	100.00±4.25	88.33±1.85	92.33±4.25	90.33±2.33	89.0±4.35	87.33±3.84
Sucrose	2000	92.0±4.04	134.33±2.90 ^b (46.01)	128.66±5.45 ^a (39.84)	117.33±4.66 ^a (27.53)	97.66±0.66(6.15)	104.16±2.48(13.21)
Acarbose	100	90.33±2.48	86.66±2.90	82.0±6.00	79.33±2.96	71.66±3.75	78.0±3.78
Crude extract	187	74.0±2.64	139.0±8.50(87.83)	72.66±6.96 ^b	71.33±0.66	75.0±4.72(1.35)	69.0±3.05
	374	72.0±3.78	119.0±10.01 ^b (65.27)	76.66±7.21 ^a (6.47)	60.33±4.63	64.0±4.50	59.0±0.57
	561	63.66±3.18	101.66±15.33 ^a (59.69)	82.0±1.52 ^a (28.80)	82.0±9.64(28.80)	72.33±6.69(13.61)	67.66±6.17(6.28)
n-hexane fraction	374	88.66±10.08	118.33±9.85 ^a (33.05)	90.33±12.17 ^a (53.65)	67.66±9.77(28.76)	78.66±11.31(46.15)	62.33±8.66(29.61)
Dichloromethane fraction	374	67.66±9.87	105.66±5.92 ^a (56.16)	86.66±10.99 ^a (28.08)	86.33±1.85 ^a (27.59)	88.33±2.02(30.54)	89.0±1.00(31.54)
Ethyl acetate fraction	374	77.66±13.64	141.0±17.08 ^a (81.56)	96.66±0.88(24.46)	82.33±7.88(6.01)	94.33±0.66(21.46)	95.33±8.00(22.75)
Methanol fraction	374	88.66±1.33	126.0±3.05 ^a (42.11)	90.0±4.93 ^a (1.51)	82.0±1.73	80.6±4.33	73.0±4.00

Data is expressed as MEAN ± SEM, Significant at ^ap<0.05, ^bp< 0.01, when compared to control. (n=6). Values in parenthesis are percentage increase in blood glucose concentrations compared to 0 min in the same group.

(170 and 374 mg/kg) and methanol-treated groups after 90 mins with the 170 mg/kg treated group having no increase in BGL post-administration of sucrose. However, lower doses (170 and 374 mg/kg) and methanol fraction had the highest sustained effects throughout the duration of the study (180 min) (Table 2).

There was 60.78% increase in blood glucose concentration 30 min following maltose administration in the control group. However, 6.97-80.94% increases in BGL were observed in the extract/fractions-treated groups. The crude extract 170-510 mg/kg significantly reduced blood glucose level though in a dose-dependent fashion after 90 min with highest dose (510

mg/kg) having 0% and middle dose (374 mg/kg) 1.74%, while dichloromethane fraction-treated group was found produced the most significant reduction in BGL among the fractions treated groups with 0% increase in BGL after 90 min. The extract (374 and 510 mg/kg) and dichloromethane fraction produced significant sustained effect throughout the duration of the study (180 min) (Table 3).

Discussion

The husk extract is used traditionally by the Ibibios of Southern Nigeria in the treatment of various ailments such as fever, convulsion, malaria, body pains, diabetes, diarrhea,

Table 3. Effect of ethanol husk extract and fractions of *Zea mays* on Blood Glucose level of rat after oral administration of maltose load

Treatment	Dose (mg/kg)	Blood Glucose Level Mg/Dl In Min					
		0 min	30 min	60 min	90 min	120 min	180 min
Control normal saline	-	100.00±4.25	88.33±1.85	92.33±4.25(1.80)	90.33±2.33(3.62)	89.0±4.35(1.55)	87.33±3.84(3.98)
Maltose	2000	82.30±2.14	132.33±1.90 ^b (60.78)	130.22±2.45(58.22)	120.66±3.22 ^a (46.60)	115.0±2.46(39.73)	106.22±4.24(29.06)
Acarbose	100	85.34±1.36	88.22±1.10(3.37)	86.0±2.20(0.77)	85.33±2.15()	84.26±1.14()	82.28±2.26()
Crude extract	187	70.0±3.46	126.66±1.85 ^b (80.94)	105.66±10.13 ^b (50.94)	61.66±5.04 ^a	72.0±3.78(2.85)	78.0±2.64(11.42)
	374	76.66±7.75	120.0±6.42 ^b (56.53)	78.0±12.00 ^a (1.74)	65.33±6.38 ^a	60.33±13.92	75.0±7.63
	561	95.66±3.71	102.33±12.01 ^a (6.97)	84.0±9.07 ^a	65.33±7.44 ^a	71.0±7.57	72.33±7.57
n-hexane fraction	374	71.33±9.82	92.33±10.17 ^b (29.44)	92.66±8.41 ^a (29.90)	68.66±4.33 ^a	83.33±6.17(16.82)	83.0±9.60(16.36)
Dichloromethane fraction	374	80.66±4.84	102.66±32.60 ^b (27.27)	80.66±2.96 ^b	79.66±4.05 ^a	83.66±0.88 ^a (3.71)	80.66±2.60
Ethyl acetate fraction	374	76.0±5.13	112.66±0.33(48.23)	120.0±6.65(57.89)	81.0±8.73(6.57)	91.0±7.78(19.73)	80.0±2.08(5.26)
Methanol fraction	374	71.0±10.06	124.0±12.74 ^b (74.64)	93.33±5.92 ^a (31.45)	74.33±2.96(4.69)	72.0±9.84(1.40)	79.66±4.41(12.19)

Data is expressed as MEAN ± SEM, Significant at ^ap<0.05, ^bp< 0.01, when compared to control. (n=6). Values in parenthesis are percentage increases in blood glucose concentrations compared to 0 min in the same group.

jaundice and hepatitis (Okokon et al., 2006). Preliminary reports showed that the husk extract possesses antidiabetic activity (Okokon et al., 2010). This work was designed to explore the possible antidiabetic mechanism of action of husk extract and fractions of *Zea mays* especially its inhibitory potentials on alpha amylase and alpha glucosidase enzymes.

The extract was found to non dose-dependently inhibit increases in blood glucose concentration following starch administration with the methanol and ethyl acetate fractions exerting the most inhibition. Complete digestion of dietary polysaccharides like starch is achieved by the combined action of α -amylases and α -glucosidase enzymes. The α -amylase enzyme digests α -bonds of the α -linked polysaccharides yielding disaccharides, like maltose, which are further reduced to monosaccharides by membrane bound α -glucosidase enzymes (Kalra, 2014; Alongi and Anese, 2018). Inhibitions of these enzymes delay the digestion of ingested carbohydrates thereby resulting in a small rise in blood glucose concentrations following carbohydrate meals as was observed in this study. As a target for managing Type 2 diabetes mellitus, many medicinal plants have been reported to possess α -amylase and α -glucosidase inhibitory potential (Ibrahim et al., 2014; Esimone et al., 2001).

Similarly, the husk extract and fractions significantly inhibited blood glucose rise when co-administered with maltose and sucrose with methanol and dichloromethane fractions exerting the highest inhibitions respectively. Acarbose, the standard drug used in this study significantly inhibited blood glucose rise when co-administered with starch, maltose and sucrose.

Alpha-amylase and α -glucosidase inhibitions by plants extracts have been reported severally (Ishnava and Metisariya, 2018; Shirwaikar et al., 2005). Phytochemicals implicated as anti-diabetic agents, do so possibly through α -amylase and glucosidase inhibition. The phytochemicals in question include flavonoids, saponins, tannins and terpenoids (Yoshikawa et al., 1998; Ortiz-Andrade et al., 2007; Ishnava and Metisariya, 2018). Phytochemicals screening of the husk extract revealed the presence of saponins, tannins, flavonoids, alkaloids and terpenes (Okokon et al., 2017). Polyphenolic compounds from plants are known to cause several effects on the biological systems which include enzymes inhibitions (Kalita et al., 2018; Funke and Melzig, 2005). The phenolic compounds are known to be strong metal ion chelators and protein precipitation agents forming insoluble complexes with proteins as well as acting as biological oxidants (Ishnava and Metisariya, 2018). Anthocyanins, a water-soluble flavonoids, have been found to be richly present in corn husk especially in polar fractions (n-butanol or methanol) of the husk (Li et al., 2008). It has been reported that anthocyanins exert inhibitory activities on alpha amylase and alpha glucosidase (Kalita et al., 2018; Berger et al., 2020; Chen et al., 2020). This may explain the high inhibitory potential of the methanol fraction as observed in this study. They are also known to exert antidiabetic activity by stimulating insulin secretion resulting in increased serum insulin levels and reduced BGL (Zhang et al., 2015).

This suggests likely involvement of insulin activity in the observed effect as diabetic rats treated with the methanol fraction of the cornhusk have been reported to have elevated serum level of insulin (Okokon and Mandu, 2018). The presence of the polyphenolic compounds in the husk extract and fractions may suggest that their inhibitory potential on α -amylase and the membrane-bound intestinal α -glucosidase enzymes may be similar to the mechanism proposed generally for the polyphenolic compounds. Furthermore, the GCMS analysis of the dichloromethane fraction revealed the presence of phytosterols such as stigmasterol and sitosterol as reported by Okokon and Mandu, (2018). These compounds have been reported to increase serum insulin levels in diabetic rats (Nuakae et al., 2015) as observed in dichloromethane husk fraction-treated diabetic rats (Okokon and Mandu, 2018). Stigmasterol and sitosterol have been reported to exert inhibitory effects on alpha amylase and alpha glucosidase (Kumar et al., 2013; Gosh et al., 2014). The presence of anthocyanin, stigmasterol and sitosterol in the husk extract and fractions may be responsible for the significant inhibitory activities observed in this study.

Conclusion

The results of this study suggest that *Zea mays* husk extract and fractions possess inhibitory activity on alpha amylase and alpha glucosidase enzymes and this maybe one of the modes of antidiabetic activity of the husk extract and fractions of *Zea mays* which can be attributed to the activities of its phytochemical constituents.

Acknowledgements

The authors are grateful to Mr Nsikan Malachy of Pharmacology and Toxicology Department for providing technical assistance.

References

- Abo KA, Fred-Jaiyesimi AA, Jaiyesimi AEA. 2008. Ethnobotanical studies of medicinal plants used in the management of diabetes mellitus in South Western Nigeria. *Journal of Ethnopharmacology*, 115:67-71.
- Alongi M, Anese M. 2008. Effect of Coffee Roasting on *in vitro* α -Glucosidase activity: inhibition and Mechanism of Action. *Food Research International*, 111:480-487.
- Berger K, Ostberg-Pottho JJ, Bakuradze T, Winterhalter P, Richling E. 2020. Carbohydrate hydrolase-inhibitory activity of juice-based phenolic extracts in correlation to their anthocyanin/copigment profile. *Molecules* 25:5224.
- Brobbe AA, Somuah-Asante S, Asare-Nkansah S, Boateng FO, Ayensu I. 2017. Preliminary phytochemical screening and scientific validation of the anti-diabetic effect of the dried husk of *Zea mays* L. (Corn, Poaceae) *International Journal of Phytopharmacy*, 7(1):01-05.
- Chen JG, Wu SF, Zhang QF, Yin ZP, Zhang L. 2020. α -Glucosidase inhibitory effect of anthocyanins from *Cinnamomum camphora* fruit: Inhibition kinetics and mechanistic insights through *in vitro* and *in silico* studies. *International Journal of Biology and Macromolecules*, 143:696-703.
- Dong J, Cai L, Zhu X, Huang X, Yin T, Fang H, Ding Z. 2014. Antioxidant activities and phenolic compounds of cornhusk, corncob and *Stigma Maydis*. *Journal of Brazilian Chemical Society*, 25:1956-1964.
- Esimone CO, Okonta JM, Ezugwu CO. 2001. Blood sugar lowering effect of *Anacardium occidentale* leaf extract in experimental rabbit model. *Journal of Natural Remedy*, 1:60-63.
- Foster S, Duke JA. 1990. *Field Guide 10 Medical Plants: Eastern and Central North America*. Houghton MifAin, Boston.
- Funke I, Melzig MF. 2005. Effect of different phenolic compounds on α -amylase activity: screening by microplate-reader based kinetic assay. *Pharmazie*, 60(10):796-797.
- Ghosh T, Ghosh S, Maity T. 2014. Antihyperglycemic activity of stigmasterol isolated from *Bacopa monnieri* Linn. aerial parts against alloxan induced diabetic rats *International Journal of Natural Products Research*, 4(2):40-46.
- Gidado A, Watafua M, Sa'ad RS, Tagi HS, Abdullahi S. 2019. Alpha-amylase, maltase and sucrase inhibitions by aqueous leaf extracts of *Anacardium occidentale* (Anacardiaceae) and *Piliostigma reticulatum* (Caesalpiniaceae) in rats. *Tropical Journal of Natural Product Research*, 3(6):210-215
- Gill LS. 1992. *Ethnomedical Uses of Plants in Nigeria*. Uniben Press, Benin, Nigeria, p: 249.
- Ibrahim MA, Koorbanally NA, Islam S. 2014. Antioxidative activity and Inhibition of Key Enzymes linked to Type 2 diabetes (α -glucosidase and α -amylase) by *Khaya senegalensis*. *Acta Pharmazie*, 64:311-324.
- Ishnava KB, Metisariya DM. 2018. *In vitro* study on α -amylase Inhibitory activity of selected ethnobotanical plant extra its and its herbal formulations. *International Journal of Pharmacognosy and Chinese Medicine*, 2(3):000136.
- Jadhav SM. 2016. Protective effect of *Zea mays* on experimentally induced gastric ulcer in rats. *Imperial Journal of Interdisciplinary Research*, 2:8.
- Kalita D, Holm DG, LaBarbera DV, Petrash JM, Jayanty SS. 2018. Inhibition of α glucosidase, α -amylase, and aldose reductase by potato polyphenolic compounds. *PLoS ONE*. 13(1):e0191025.

- Kalra S. 2014. Alpha Glucosidase Inhibitors. Journal Of Pakistan Medical Association, 64(4):474-476.
- Karan SK, Mishra SK, Pal DK, Mondal A. 2012. Isolation of β -sitosterol and evaluation of antidiabetic activity of *Aristolochia indica* in alloxan induced diabetic mice with reference to in-vitro antioxidant activity. Journal of Medicinal Plant Research, 6:1219-1223
- Kumar S, Kumar V, Prakash O. 2013. Enzymes inhibition and antidiabetic Effect of Isolated Constituents from *Dillenia indica*. BioMed Research International. Volume 2013, Article ID 382063, 7 pages <http://dx.doi.org/10.1155/2013/382063>.
- Li CY, Kim HW, Won SR, Min HK, Park KJ, Park Jy, Ahn MS, Rhee H. 2008. Corn husk as a potential source of anthocyanins. Journal of Agricultural Food and Chemistry, 56(23):11413-11416.
- Nualkaew S, Padee P, Talubmook C. 2015. Hypoglycemic activity in diabetic rats of stigmasterol and sitosterol-3- β -D-glucopyranoside isolated from *Pseuderanthemum palatifurum* (Ness) Radlk. leaf extract. Journal of Medicinal Plant Research, 9(20):629-635.
- Ogawa K, Takeuchi M, Nakamura N. 2005. Immunological effects of partially hydrolysed arabinoxylan from corn husk in mice. Biosciences, Biotechnology and Biochemistry, 69:19-25.
- Okokon JE, Antia BS, Mohanakrishnan D, Sahal D. 2017a. Antimalarial and antiplasmodial activities of *Zea mays* husk. Pharmaceutical Biology, 55(3):1394-1400.
- Okokon JE, Nelson E, Sunday M. 2016. Antidepressant activity of ethanol husk extract of *Zea mays*. Advance Herbal Medicine, 2(4):22-28.
- Okokon JE, Nelson E, Sunday M. 2016. Antidepressant activity of ethanol Husk extract of *Zea mays*. Advanced Herbal Medicine, 2(4): 22-28.
- Okokon JE, Nyong M. 2018. Antidiabetic and hypolipidemic activities of *Zea mays* husk extract and fractions. Journal of Herbs Spices and Medicinal Plants, 24(3):1-17.
- Okokon JE, Nyong ME, Essien GE, Nyong E. 2017b. Nephroprotective activity of husk extract and fractions of *Zea mays* against alloxan-induced oxidative stress in diabetic rats. Journal of Basic Pharmacology and Toxicology, 1(3):1-10.
- Okokon JE, Nyong ME, Essien GE, Nyong E. 2017c. Hepatoprotective activity of husk extract and fractions of *Zea mays* against alloxan-induced oxidative stress in diabetic rats. International Journal of Herbal Medicine, 5(4):43-50.
- Okokon JE, Nyong ME, Thomas P, Udobang JA, Enin G. 2021. Antiobesity activities of extract, fractions and pure compounds from husk of *Zea mays*. Tropical Journal of Natural Products Research, 5(10):1868-1875.
- Okokon JE, Nyong ME, Thomas P, Udobang JA, Enin G. 2021. Antiobesity activities of extract, fractions and pure compounds from husk of *Zea mays*. Tropical Journal of Natural Products Research, 5(10):1868-1875.
- Okokon JE, Obot J, Amazu LU. 2018. Antiulcerogenic activity of husk extract of *Zea mays*. African Journal of Pharmacology and Therapeutics, 7(2):41-45.
- Okokon JE, Udobang JA, Bassey AL, Edem UA, Agu CE. 2020. Hepatoprotective and nephroprotective activities of *Zea mays* husk extract against paracetamol-induced liver and kidneys injuries in rats. Tropical Journal of Natural Products Research 4(3):69-76.
- Okokon JE, Udobang JA, Obot D, Agu CE. 2019. Nephroprotective activity of *Zea mays* husk extract against gentamicin- induced kidney injury in rats. Journal of Medicinal Plant Studies, 7(6):156-160.
- Ortiz-Andrade RR, García-Jiménez S, Castillo-España P, Ramírez-Avila G, Villalobos-Molina R, Estrada-Soto S. 2007. Alpha-glucosidase inhibitory activity of the methanolic extract from *Tournefortia hartwegiana*: An anti-hyperglycemic agent. Journal of Ethnopharmacology, 109:48-53.
- Owoyele BV, Negedu MN, Olaniran SO, Onasanwo SA, Oguntoye SO, Sanya JO, Oyeleke SA, Ibidapo AJ, Soladoye A. O, 2010. Analgesic and anti-inflammatory effects of aqueous extract of *Zea mays* husk. Journal of Medicinal Food, 13(2):343-347.
- Ramírez-Avila G, Villalobos-Molina R, Estrada-Soto S. 2007. Alpha-Glucosidase Inhibitory Activity of the Methanolic Extract from *Tournefortia hartwegiana*: An Anti-hyperglycemic Agent. Journal of Ethnopharmacology, 109:48-53.
- Shirwaikar A, Rajendran K, Punitha ISR. 2005. Antidiabetic activity of alcoholic stem extract of *Coscinium fenestratum* in streptozotocin nicotinamide-induced Type 2 diabetic rats. Journal of Ethnopharmacology, 93:369-374.
- Simmonds NW. 1979. Evolution of Crop Plants. Longman. London, pp. 128-129.
- Udobang JA, Okokon JE, Obot D, Agu CE. 2019. Hepatoprotective activity of *Zea mays* husk extract against carbon tetrachloride induced liver injury in rats. Research Journal of Life Sciences, Bioinformatics, Pharmaceutical And Chemical Sciences, 5(5):82-94.
- WHO expert committee on diabetes mellitus. Tech. Rep. Series No.646. World Health Organisation, Geneva, 1980.
- World Health Organization. Glucose analyser. Core medical equipment information. 2011.

www.who.int/medical_devices/en/index.html. Assessed on 3rd June, 2019.

- Yoshikawa M, Murakami T, Yashiro K, Matsuda H. 1998. Kotalanol, a potent alpha-glucosidase inhibitor with thiosugar sulfonium sulfate structure from antidiabetic agurvedic medicine *Salacia reticulata*. Chemical and Pharmaceutical Bulletin (Tokyo), 46:1339-1340.
- Zhang Y, Wu L, Ma Z, Cheng J, Liu J. 2016. Antidiabetic, antioxidant and antihyperlipidemic activities of flavonoids from corn silk on STZ-induced diabetic mice. Molecules, 21(1):1-11.