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In vitro antioxidant and antidiarrheal activities of aqueous and *n*-hexane extracts of *Cucurbita maxima* seed in castor oil-induced diarrheal rats

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ABSTRACT: Diarrhea is a common health complaint occurring with mild, temporary conditions to a potentially life-threatening condition. *Cucurbita maxima* (Cucurbitaceae) seed is reportedly used traditionally for the treatment of diarrheal and thus this study aimed to evaluate the *in vitro* antioxidants, total tannins, phenolics contents, and antidiarrheal potentials of *n*-hexane and aqueous *C. maxima* seed extracts in castor-oil induced diarrheal rats. The *n*-hexane extract mainly contains oils while the aqueous extract was thick, brown solid. The aqueous and *n*-hexane seed extract of *C. maxima* expressed significant 2,2, diphenyl-1-picrythdrazyl (DPPH) scavenging activities at 6.25 – 1000 mg/mL with IC_{50} values of 104.01 mg/mL, 29.27 mg/mL and 26.78 mg/mL for *n*-hexane, aqueous and vitamin C respectively. The hydroxyl radical scavenging activities of the *n*-hexane and aqueous seed extract of *C. maxima* were significantly lower at higher concentrations compared with that of vitamin C. Furthermore, the total antioxidant capacities of *n*-hexane (22.08mg/mL) and aqueous seed extract (11.03 mg/mL) of *C. maxima* were found to be higher than that of vitamin C (134.46 mg/mL). The aqueous extracts (658.33±380.08 mg QE/g) total tannins were not significantly different from the *n*-hexane extract (468.33±102.55 mg QE/g) while the *n*-hexane extract contains significantly higher total phenolics (2.93±1.25 mg GAE/g) compared with the aqueous extract (0.19±0.04 mg GAE/g). Percentage inhibition of stooling was found to be 57±22%, 41±16%, and 46±11% for loperamide, *n*-hexane, and aqueous respectively. The study concludes that aqueous and *n*-hexane seed extracts of *C. maxima* (pumpkin) possess *in vitro* antioxidant activities and antidiarrheal properties.

1. INTRODUCTION

Cucurbita maxima (pumpkin) is a member of the Cucurbitaceae family of plants. In addition to having medical and nutritional benefits, pumpkin is a commercially important vegetable crop (El-Aziz et al., 2011; Kaur et al., 2020). Pumpkins are squash-like fruit that has different size ranges (Orsolek et al., 2000). They are eaten as food and medicinally important (Kaur et al., 2020). All parts pumpkin contain important bioactive components including β-carotene, vitamins (thiamine, riboflavin, K and B6), moderate amount of carbohydrates and minerals (selenium, potassium, phosphorus, magnesium and iron) (Rakcejeva et al., 2011). The seeds are edible with rich protein content and are used as food supplements due to high content of micro and macro minerals such as zinc, phosphorus, manganese, magnesium, copper and calcium (Kaur et al., 2020). Medicinally, pumpkins prevent chronic ailments, possess glucose-lowering activity, antioxidation, antilipogenic effect, anti-inflammation, anticarcinogenic and antiangiogenesis (Caili et al., 2006; Kaur et al., 2020; Wang et al., 2012).

Diarrhea is a common health complaint, with temporary mild condition to a potentially life-threatening condition. Diarrheal is characterized by an abnormal loose or watery stool, which are usually caused by infections with parasites, viruses or bacteria. The conditions are due to imbalanced occurring in the secretory or absorptive physiologies of electrolyte and water (Whyte & Jenkins, 2012). Some pathogenic agents, such as enteropathogenic bacteria, Giardia and cryptosporidium are causes of persistent diarrhea (Shrivastava et al., 2020). The treatments of diarrhea are often done using medications which inhibits prostaglandin secretions, antisecretory and antispasmodic drugs, such as loperamide, atropine and diaretyl (Agbor et al., 2014; Rang et al., 2007). Some of these medications are associated with side effects such as drowsiness, constipation, and colorectal cancer (Rang et al., 2007). In some rural areas, with little access to these medications, plant and plant products are used in management of diarrhea gastrointestinal disorders (Sebai et al., 2014). This study was design to evaluate

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the *in vitro* antioxidant and antidiarrheal activities of *C. maxima* (pumpkin) seed, which is used in the management of diarrhea.

2. MATERIALS AND METHODS

2.1. Chemicals and Drugs

2,2, diphenyl-1-picrythdrazyl (DPPH), H_2O_2, *n*-hexane, ascorbic acid, $FeCl_3$, H_2SO_4, gallic acid, HCl, glacial acetic acid, sodium phosphate, ammonium molydate were obtained from M&B, England. Castor oil was purchased from of El Hawag, Egypt. Loperamide hydrochloride was purchased from Zunamediks, Nigeria. The rest of the chemicals are of analytical quality.

2.2. Plant Material and Preparation

C. maxima (pumpkin) seed were purchased from Azare market, Katagum Local Government, Bauchi State, Nigeria and identified at the Department of Biological Sciences, Bauchi State University, Gadau, Nigeria. The pumpkin seed were grounded using a pestle and mortar. The oil was extracted with *n*-hexane at room temperature by weighing 20 g of the powder seed in 250 mL of *n*-hexane for 24 hours in an airtight stopped glass container, after which the filtered shaft from the *n*-hexane extract were dissolve in 250 mL of water for 24 hours. The filtrates were then concentrated separately using a rotary evaporator at 40^0C to obtain the *n*-hexane extract and aqueous extracts respectively.

2.3. *In vitro* Antioxidant Assay

The methods of Mccune and Johns (2002); Smirnoff and Cumbes (1989), and Ruch et al. (1989) were used to evaluate the DPPH, hydroxyl (-OH) and H_2O_2 radical scavenging activities of the extracts respectively. The method of Prieto et al. (1999) was used to evaluate the total antioxidant capacity of the extracts. The methods of Belguidoum et al. (2015), using Folic-ciocalteu was used to determine the total phenolic contents (TPC).

2.4. Animal Care

Adult albino rats were obtained from the animal holding unit, Department of Pharmacology Bauchi State University, Gadau, Nigeria. The animals were housed in standard plastic cages and acclimatized for a period of 2 weeks. They were given unlimited access to animal chaw and water.

2.5. Induction of Diarrheal

Diarrheal was induced in twelve (12) adult albino rats with average weight of 148±10 g by oral administration of 0.5 – 1.0 mL of castor oil after an overnight fasting for 12 hours (Elisha et al., 2013).

2.6. Animal Grouping and Administration for Antidiarrheal Study

The antidiarrheal activities of the *n*-hexane and aqueous *C. maxima* seed extracts was evaluated by randomly distributing of the animals into 5 groups of 3 animals each. Group one was neither diarrheal induced nor received any treatment. Groups 2 and 3 were diarrheal induced animals, which served as the negative and positive control groups and received 1 mL of castor oil and 3 mg/kg bwt of loperamide respectively. Groups 4 and 5 were diarrheal induced animals, which served as test groups and received 500 mg/kg bwt of the *n*-hexane and aqueous *C. maxima* seed extracts respectively. All treatment was administered 30 minutes after diarrheal induction and the animals were monitored for up to 4 hours. The faeces (stools) were collected and counted after 2 and 4 hours respectively. The numbers of wet stool passed out were compared with control group.

2.7. Statistical analysis

The data were analysed using one-way ANOVA and the Duncan multiple range test. Data are presented as mean standard deviation (SD). The GraphPad Prism 6 programme was used to create the graphs. The SPSS vs 20, SPSS Inc., Chicago. IL, USA and GraphPad Prism, California, USA were used for the statistical analysis.

3. RESULTS

3.1. Antioxidant Activities of *C. maxima* Seed Extracts

The *n*-hexane and aqueous seed extract of *C. maxima* expressed significant DPPH scavenging activities for various concentration range of 6.25 – 1000 mg/mL (Table 1). The DPPH IC_{50} values were 104.01 mg/mL, 29.27 mg/mL and 26.78 mg/mL for *n*-hexane, aqueous and vitamin C respectively (Figure 1). The hydroxyl radical scavenging activities of the *n*-hexane and aqueous seed extract of *C. maxima* were significantly lower at higher concentrations compared with that of vitamin C (Figure 2). However, the hydrogen peroxide scavenging activities of aqueous seed extract (50.03 mg/mL) was higher than that of the *n*-hexane extract (129.20 mg/mL) (Figure 3). Furthermore, the total antioxidant capacities of *n*-hexane (22.08 mg/mL) and aqueous seed extract (11.03mg/mL) of *C. maxima* were found to be higher than that of vitamin C (134.46 mg/mL) (Figure 4). The aqueous extracts (658.33±380.08 mg QE/g) total tannins were not significantly different from the *n*-hexane extract (468.33±102.55 mg QE/g) while the *n*-hexane extract contains significantly higher total phenolics (2.93±1.25 mg GAE/g) compared with the aqueous extract (0.19±0.04 mg GAE/g) (Figure 5 and 6).

3.2. Effects of *n*-Hexane and Aqueous *C. maxima* Seed Extracts in Castor Oil-Induced Diarrheal Rats

The aqueous extract of the seed of *C. maxima*, castor oil and loperamide treated diarrheal animal showed increased number of stooling (Table 2). The percentage inhibition of the stooling was found to be 37.50%, 33.33% and 100.00% respectively in the experiment for loperamide when compared with the castor oil diarrheal induced without treatment. While the *n*-hexane and aqueous extract of the seed of *C. maxima* expressed 12.50%, 44.44%, 66.67% and 37.50%, 66.67%, 33.33% respectively for 500 mg/kg body weight of the seed compared with the castor oil diarrheal induced without treatment. The average percentage inhibition of stooling was found to be 57±22%, 41±16% and 46±11% for loperamide (3 mg/kg bwt), *n*-hexane (500 mg/kg bwt) and aqueous (500 mg/kg bwt) respectively.

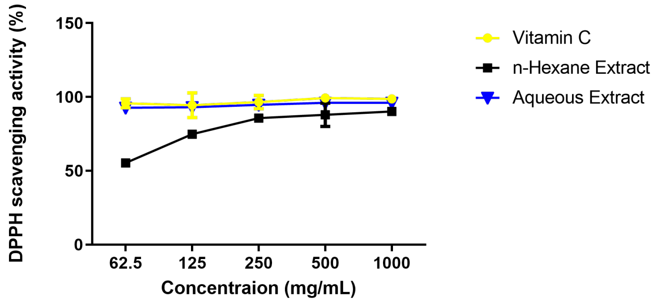

Figure 1. DPPH radical scavenging activities of *n*-hexane and aqueous *Cucurbita maxima* seed extracts. Values are means ± SD of triplicate determinations

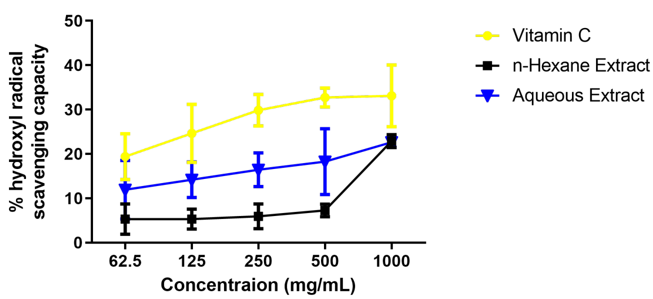

Figure 2. Hydroxyl (^{-}OH) radical scavenging activities of *n*-hexane and aqueous *Cucurbita maxima* seed extracts. Values are means ± SD Values are means ± SD (n=3)

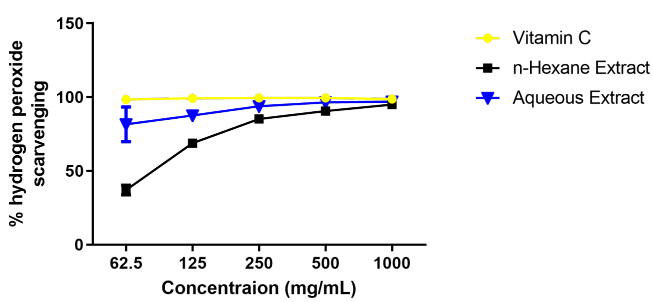

Figure 3. Hydrogen peroxide (H_2O_2) radical scavenging activities of *n*-hexane and aqueous *Cucurbita maxima* seed extracts. Values are means ± SD (n=3)

4. DISCUSSION

Antioxidant characteristics are critical in determining the antioxidant activity of therapeutic plants (Xu et al., 2017). Both ROS and RNS have been implicated in several physiological

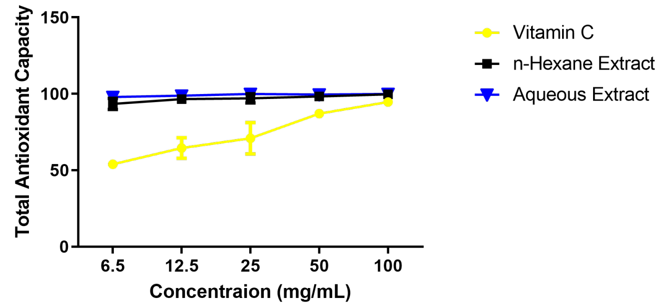

Figure 4. Total Antioxidant capacity of *n*-hexane and aqueous *Cucurbita maxima* seed extracts. Values are means ± SD Values are means ± SD (n=3)

Table 1
IC_{50} values for various *in vitro* antioxidant activity of *n*-hexane and aqueous *Cucurbita maxima* seed extracts

IC_{50} (mg/mL)				
Samples	**DPPH**	**^{-}OH**	**H_2O_2**	**TAC**
Vitamin C	26.78	>1000	13.22	134.46
n-hexane Extract	104.01	>1000	129.20	22.08
Aqueous Extract	29.27	>1000	50.03	11.03

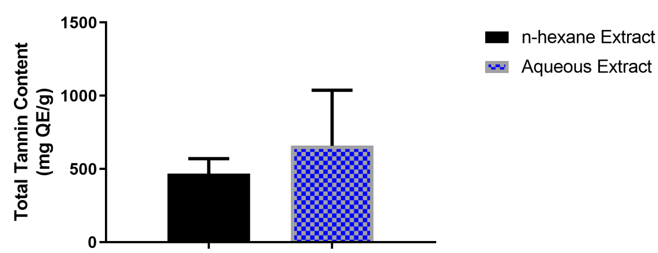

Figure 5. Total tannin content of *n*-hexane and aqueous *Cucurbita maxima* seed extracts. Values are means ± SD of triplicate determinations

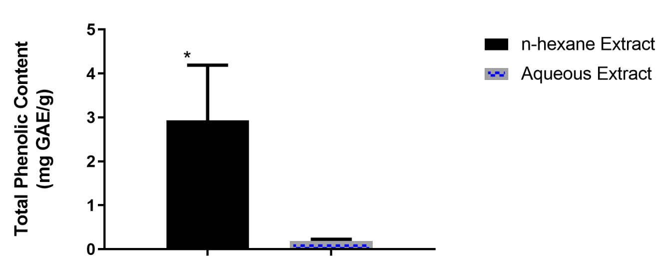

Figure 6. Total phenolic content of *n*-hexane and aqueous Cucurbita maxima seed extracts. Values are means ± SD of triplicate determinationsValue with superscript (*) are significantly high at $p<0.05$

Table 2
Antidiarrheal activities of *n*-hexane and aqueous *Cucurbita maxima* seed extracts in castor oil induced diarrhea rats

Groups	1^{st} experiment No. of stools	2^{nd} experiment No. of stools	3^{rd} experiment No. of stools	% of inhibition			Average
Control	5.00	5.00	7.00	—-	—-	—-	—-
Castor oil	8.00	9.00	8.00	0.00	0.00	0.00	0.00
Loperamide (3 mg/kg bwt)	11.00	6.00	6.00	37.50	33.33	100.00	57±22
n-HEX (500 mg/kg bwt)	9.00	5.00	2.00	12.50*	44.44*	66.67*	41±16
AQE (500 mg/kg bwt)	5.00	15.00	2.00	37.50	66.67*	33.33*	46±11

n-HEX = *n*-Hexane extract, AQE = Aqueous extract, mg/kg bwt = mg per kg body weight, Values with * are significantly different at p<0.05 from reference compound

and pathological conditions, and could further involved in disease progression as in diabetic mellitus, atherosclerosis and cardiovascular diseases (Forrester et al., 2018; Liao & Yin, 2000). ROS have been identified as one of the key players in the development of cancer's various hallmarks. Because ROS are linked to all stages of cancer (Kwon et al., 2019). Recently, Casas et al. (2020) suggested that ROS can be used for numerous key signalling and metabolic processes at any concentration. Nevertheless, ROS remain an important parameter for the evaluation of antioxidants activities (Munteanu & Apetrei, 2021). Imbalance between antioxidant activity and free radical activity (Oxidative stress) is also known to contribute to various gastrointestinal malignancies including gastric and gastrointestinal diseases, including gastroduodenal ulcer (Kekec et al., 2009; Peng et al., 2008). Important *in vitro* antioxidant assays used in assessing the antioxidant status of medicinal plants include DPPH, hydroxyl radical (^{-}OH), hydrogen peroxide (H_2O_2) and total antioxidant capacity (TAC) as reported in several studies (Munteanu & Apetrei, 2021; Tijjani, Mohammed, Ahmed, et al., 2020; Tijjani, Mohammed, Muktar, et al., 2020) . *n*-hexane and aqueous *C. maxima* seed extracts demonstrated potent *in vitro* antioxidant activities, which are comparable with vitamin C in DPPH scavenging and TAC. However, a lower potency was observed in hydroxyl radical and hydrogen peroxide scavenging activities compared with vitamin C. This suggests that the extracts scavenge hydroxyl radicals at a lower capacity. In vivo, H_2O_2 are rapidly decomposed into water and oxygen, preventing the deleterious effects of hydroxyl radical, which can initiate lipid peroxidation and DNA damage (Poljsak et al., 2013; Topal et al., 2015). Plant contains secondary metabolites, which are responsible for several of their biological activities (Tijjani, Adegunloye, et al., 2020; Tijjani et al., 2018). These secondary metabolites are similarly associated with the antioxidant activities of many plants. Flavonoids are for example strong antioxidant compounds (Tijjani et al., 2018). Flavonoids, saponins and triterpenoids are reported to possess the property to inhibit intestinal motility and hydro electrolytic secretions, which are properties altered in diarrheal conditions (Gaginella & Phillips, 1975). In the present study, the higher contents of total phenolic content in hexane extract compared with aqueous extract did not reflect in the *in vitro* antioxidant status at higher concentration (Figure 1, 2, 3 and 4). The concentration of phenolic may be from the difference in polarity of solvent used in the extraction (Jing et al., 2015). Antidiarrheal medicinal plants are also known to possess antioxidant, antibacterial, and anti-inflammatory properties (Tzung-Hsun et al., 2005).

Diarrhea is a common health problem in most developing countries, especially where there are poor sanitation or hygiene. Diarrhea is the increase in number, fluidity and presence of blood and increased neutrophil polymorphs in the stools (Bern et al., 1992). The model used in the study of antidiarrheal involves the induction of diarrheal in experimental animals using castor oil. The mechanism of induction involves ricinoleic acid, which is the active compound for induction of diarrheal in castor oil. Ricinoleic acid causes inflammation of the intestinal mucosa, leading to increased prostaglandin release, increased peristalsis, and reduced reabsorption of chloride (Cl^{-}), potassium (K^{+}) and sodium (Na^{+}) ions as well as reduced reabsorption of water from the gut, decreased Na^{+},K^{+} ATPase activities in the small intestine and colon, leading to diarrhea (Gaginella & Phillips, 1975; Galvez et al., 1993; Gutiérrez et al., 2014). Other mechanisms reported to involve include activation of adenylate cyclase, mucosal cAMP-mediated active secretion, platelet activating factor and alterations of nitric oxide synthetase pathway (Capasso et al., 1994; Mascolo et al., 1996; Pinto et al., 1992). Diarrheas are treated using drugs like loperamide. Loperamide antidiarrheal activity is linked to inhibition of peristalsis (Fujita et al., 2014; Scarpellini et al., 2016).

The present study on the antidiarrheal activities of *n*-hexane and aqueous *C. maxima* seed extracts in castor induced diarrheal rats indicated that the extracts from *C. maxima* seed significantly inhibited the formation of diarrheal stools in castor oil induced diarrheal rats. Their antidiarrheal activities are comparable with the reference drug loperamide. The antidiarrheal activities of the seed oil and extract maybe attributed to protection against gastric irritation, inflammation and reduced prostaglandin release (Ramasamy et al., 2016; Umukoro & Ashorobi, 2005). The antidiarrheal properties may also be link to the rich phytochemical contents of the seed oil and extract (Han et al., 2014; Otshudi et al., 2000; Venkatesan et al., 2005). Flavonoids, for example are reported to inhibit the release of autacoids and prostaglandins, thus inhibiting the motility and secretion induced by castor oil in the rats (Hasan et al., 2009). Several studies with medicinal plants have also shown that their antidiarrheal properties are associated with stimulation of water reabsorption, reduced electrolyte secretion, intestinal motility and stimulate antispasmodic effects (Agbor et al., 2004; Kambaska et al., 2006; Lozoya et al., 2002; Oben et al., 2006).

5. CONCLUSION

The study concludes that *n*-hexane and aqueous *C. maxima* (pumpkin) seed extracts possess *in vitro* antioxidant activities, they contain appreciable total tannins and total phenolics contents. Furthermore, *n*-hexane and aqueous *C. maxima* (pumpkin) seed extracts possess significant antidiarrheal properties. Further studies are needed to validate the antidiarrheal activities of *C. maxima* using charcoal meal intestinal transit and laxative test as well as identifying their active antidiarrheal principles through an activity-guided fractionations and GCMS analysis.

6. CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest associated with this research work.

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ETHICAL APPROVAL

The University of Jos Ethical Review Committee accepted the research with the reference number UJ/FPS/F17-00379.

AUTHOR CONTRIBUTIONS

HT, AIM, MMY, ELA, AS - Research concept and design; HT, AIM, MMY, ELA, AS - Collection and/or assembly of data; HT, AIM, MMY, ELA, AS - Data analysis and interpretation; HT, AIM, MMY, ELA, AS - Writing the article; HT, AIM - Critical revision of the article, HT, AIM, MMY, ELA, AS - Final approval of the article.

REFERENCES

Agbor, G.A., Longo, F., Makong, E.A., Tarkang, P.A., 2014. Evaluation of the antidiarrheal and antioxidant properties of Justicia hypocrateriformis. Pharmaceutical Biology. 52(9), 1128–1133. https://doi.org/10.3109/13880209.2013.879189

Agbor, G.A., Talla, L., Ngogang, J.Y., 2004. The antidiarrhoeal activity of Alchornea cordifolia leaf extract. Phytotherapy Research. 18, 873–879. https://doi.org/10.1002/ptr.1446

Belguidoum, M., Dendougui, H., Kendour, Z., 2015. In vitro antioxidant properties and phenolic contents of Zygophyllum album L. from Algeria. Journal of Chemical and Pharmaceutical Research. 7(1), 510–514.

Bern, C., Martines, J., Dezoysa, I., Glass, R.I., 1992. The magnitude of the global problem of diarrheal disease.

Caili, F.U., Huan, S., Quanhong, L.I., 2006. A review on pharmacological activities and utilization technologies of pumpkin. Plant Foods for Human Nutrition. 61(2), 70–77. https://doi.org/10.1007/s11130-006-0016-6

Capasso, F., Mascolo, N., Izzo, A.A., Gaginella, T.S., 1994. Dissociation of castor oil-induced diarrhea and intestinal mucosal injury in rat: effect of NGnitro- L-arginine methyl ester. British Journal of Pharmacology. 113, 1127–1130. https://doi.org/10.1111/j.1476-5381.1994.tb17113.x

Casas, A.I., Nogales, C., Mucke, H.A., Petraina, A., Cuadrado, A., Rojo, A.I., Ghezzi, P., Jaquet, V., Augsburger, F., Dufrasne, F., 2020. On The Clinical Pharmacology Of Reactive Oxygen Species. Pharmacological Reviews. 72, 801–828. https://doi.org/10.1124/pr.120.019422

El-Aziz, A., El-Kalek, A.B., A., 2011. Antimicrobial protein and oil seed from pumpkin (Cucurbita moschata). Nature and Science. 9(3), 105–119.

Elisha, I.L., Makoshi, M.S., Makama, S., Dawurung, C.J., Offiah, N.V., Gotep, J.G., 2013. Antidiarrheal evaluation of aqueous and ethanolic stem bark extracts of Khaya senegalensis A. Juss (Meliaceae) in albino rats. Pakistan Veterinary Journal. 33, 32–38.

Forrester, S.J., Kikuchi, D.S., Hernandes, M.S., Xu, Q., Griendling, K.K., 2018. Reactive Oxygen Species In Metabolic And Inflammatory Signaling. Circulation Research. 122, 877–902. https://doi.org/10.1161/CIRCRESAHA.117.311401

Fujita, W., Gomes, I., Dove, L.S., Prohaska, D., Mcintyre, G., Devi, L.A., 2014. Molecular characterization of eluxadolineas a potential ligand targeting mu-delta opioid receptor heteromers. Biochemical Pharmacology. 92(3), 448–456. https://doi.org/10.1016/j.bcp.2014.09.015

Gaginella, T.S., Phillips, S.F., 1975. Ricinoleic acid: Current view of an ancient oil. Digestive Diseases. 20, 1171–1177. https://doi.org/10.1007/BF01070759

Galvez, J., Zavzuelo, A., Crespo, M.E., Lorente, M.D., Ocete, M.A., Jimenez, J., 1993. Anti-diarrhoeic activity of Euphorbia hirta extract and isolation of an active flavonoid constituent. Planta Medica. 59, 333–336. https://doi.org/10.1055/s-2006-959694

Gutiérrez, S.P., Mendoza, D.Z., Peredo, C.S., Sánchez, O.S., Sánchez, M.A.Z., 2014. Evaluation of the anti-diarrheal activity of Salvia connivens. Pharmaceutical Biology. 52(11), 1467–1470. https://doi.org/10.3109/13880209.2014.898076

Han, X., Pang, Y., Liu, S., 2014. Antidiarrhea and antioxidant activities of honokiol extract from Magnoliae officinalis cortex in mice. Tropical Journal of Pharmaceutical Research. 13(10), 1643–1651. https://doi.org/10.4314/tjpr.v13i10.11

Hasan, R., Hossain, M., Akter, R., Jamila, M., Mazumder, M.E.H., Islam, I., 2009. Antioxidant, antidiarrhoeal and cytotoxic properties of Punica granatum Linn. Latin American Journal of Pharmacy. 28(5), 783–788.

Jing, L., Ma, H., Fan, P., Gao, R., Jia, Z., 2015. Antioxidant potential, total phenolic and total flavonoid contents of Rhododendron anthopogonoides and its protective effect on hypoxia-induced injury in PC12 cells. BMC Complementary and Alternative Medicine. 15(1), 287. https://doi.org/10.1186/s12906-015-0820-3

Kambaska, K.B., Purandra, M., Dayanidhi, M., 2006. Green leaves of diarrhoeal diseases used by the tribal of Kenojhar and Mayurbhanj district of Orissa, India. Ethnobot Leaflets. 10, 305–321.

Kaur, S., Panghal, A., Garg, M.K., Mann, S., Khatkar, S.K., Sharma, P., Chhikara, N., 2020. Functional and nutraceutical properties of pumpkin - a review. Nutrition and Food Science. 50(2), 384–401. https://doi.org/10.1108/NFS-05-2019-0143

Kekec, Y., Paydas, S., Tuli, A., Zorludemir, S., Sakman, G., Seydauglu, G., 2009. Antioxidant levels in cases with gastrointestinal cancer.

European Journal of Internal Medicine. 20, 403–406. https://doi.org/10.1016/j.ejim.2008.12.003

Kwon, S., Ko, H., You, D.G., Kataoka, K., Park, J.H., 2019. Nanomedicines For Reactive Oxygen Species Mediated Approach: An Emerging Paradigm For Cancer Treatment. Accounts Of Chemical Research. 52, 1771–1782. https://doi.org/10.1021/acs.accounts.9b00136

Liao, K.L., Yin, M.C., 2000. Individual and combined antioxidant effects of seven phenolic agents in human erythrocyte membrane ghosts and phosphatidylcholine liposome systems: Importance of the partition coefficient. Journal of Agricultural and Food Chemistry. 48, 2266–2270. https://doi.org/10.1021/jf990946w

Lozoya, X., Reyes-Morales, H., Chavez-Soto, M.A., 2002. Intestinal anti-spasmodic effect of a phytodrug of Psidium guajava folia in the treatment of acute diarrheic disease. Journal of Ethnopharmacology. 83, 19–24. https://doi.org/10.1016/S0378-8741(02)00185-X

Mascolo, N., Izzo, A.A., Gaginella, T.S., Capasso, F., 1996. Relationship between nitric oxide and platelet activating factor in castor oil-induced mucosal injury in the rat duodenum. Naunyn-Schmiedeberg's Archives of Pharmacology. 353, 680–684. https://doi.org/10.1007/BF00167187

Mccune, L.M., Johns, T., 2002. Antioxidant activity in medicinal plants associated with the symptoms of diabetes mellitus used by the indigenous peoples of the North American boreal forest. Journal of Ethnopharmacology. 82, 197–205. https://doi.org/10.1016/S0378-8741(02)00180-0

Munteanu, I.G., Apetrei, C., 2021. Analytical Methods Used In Determining Antioxidant Activity: A Review. International Journal Of Molecular Sciences. 22, 3380–3380. https://doi.org/10.3390/ijms22073380

Oben, J.E., Assi, S.E., Agbor, A.G., Musoro, D.F., 2006. Effect of Eremomastax speciosa on experimental diarrhea. African Journal of Traditional, Complementary and Alternative Medicines. 3, 95–100. https://doi.org/10.4314/ajtcam.v3i1.31144

Orsolek, M., George, D., Greaser, L., Jayson, Harper, K., 2000.

Otshudi, A.L., Vercruysse, A., Foriers, A., 2000. Contribution to the ethnobotanical, phytochemical and pharmacological studies of traditionally used medicinal plant in the treatment of dysentery and diarrhea in Lomela area, Democratic Republic of Congo (DRC). Journal of Ethnopharmacology. 71(3), 411–423. https://doi.org/10.1016/S0378-8741(00)00167-7

Peng, Y.C., Hsu, C.L., Tung, C.F., Chou, W.K., Huang, L.R., Hung, D.Z., Hu, W.H., Yang, D.Y., 2008. Chemiluminescence assay of mucosal reactive oxygen species in gastric cancer, ulcer and antra mucosa. Hepatogastroenterology. 55, 770–773.

Pinto, A., Autore, G., Mascolo, N., Sorrentino, R., Biondi, A., Izzo, A.A., Capasso, F., 1992. Time course of PAF formation by gastrointestinal tissue in rats after castor oil challenge. Journal of Pharmacy and Pharmacology. 44, 224–226. https://doi.org/10.1111/j.2042-7158.1992.tb03586.x

Poljsak, B., Šuput, D., Milisav, I., 2013. Achieving The Balance Between Ros And Antioxidants: When To Use The Synthetic Antioxidants. Oxidative Medicine And Cellular Longevity. 2013, 956792. https://doi.org/10.1155/2013/956792

Prieto, P., Pineda, M., Aguilar, M., 1999. Spectrophotometric quantitation of antioxidant capacity through the formation of a phosphomolybdenum complex specific application to the determination of vitamin E. Analytical Biochemistry. 269(2), 337–341. https://doi.org/10.1006/abio.1999.4019

Rakcejeva, T., Galoburda, R., Cude, L., Strautniece, E., 2011. Use of dried pumpkins in wheat bread production. Procedia Food Science. 1, 441–447. https://doi.org/10.1016/j.profoo.2011.09.068

Ramasamy, A., Das, S., Mani, V., Sengottuvelu, S., Prabhu, V.V., 2016. Evaluation of Anti-diarrheal Potential of Hydroalcoholic Extracts of Leaves of Murrayakoenigii in Experimental Animals. Journal of Dietary Supplements. 13(4), 393–401. https://doi.org/10.3109/19390211.2015.1101636

Rang, H.P., Dale, M.M., Ritter, J.M., Moore, R.K., 2007. Rang & Dale's Pharmacology, and others, (Eds.). Elsevier, Edinburgh, p. 808.

Ruch, R.J., Cheng, S.J., Klaunig, J.E., 1989. Prevention of cytotoxicity and inhibition of intercellular communication by antioxidant catechins isolated from Chinese green tea. Carcinogenesis. 10, 1003–1008. https://doi.org/10.1093/carcin/10.6.1003

Scarpellini, E., Laterza, L., Ianiro, G., Tack, J., Abenavoli, L., Gasbarrini, A., 2016. Eluxadoline for the treatment of diarrhea predominant irritable bowel syndrome. Expert Opinion on Pharmacotherapy. 17(10), 1395–1402. https://doi.org/10.1080/14656566.2016.1182982

Sebai, H., Jabri, M.A., Souli, A., 2014. Antidiarrheal and antioxidant activities of chamomile (Matricaria recutita L.) decoction extract in rats. Journal of Ethnopharmacology. 152(2), 327–332. https://doi.org/10.1016/j.jep.2014.01.015

Shrivastava, A.K., Mohakud, N.K., Panda, S., Patra, S.D., Kumar, S., Sahu, P.S., 2020. Major enteropathogens in humans, domestic animals, and environmental soil samples from the same locality: prevalence and transmission considerations in coastal Odisha, India. Epidemiology and Health. 42. https://doi.org/10.4178/epih.e2020034

Smirnoff, N., Cumbes, Q.J., 1989. Hydroxyl radical scavenging activity of compatible solutes. Phytochemistry. 28, 1057–1060. https://doi.org/10.1016/0031-9422(89)80182-7

Tijjani, H., Adegunloye, A.P., Uba, H., Joel, E.B., Olatunde, A., 2020. Antioxidant activities of aqueous and ethyl acetate fractions of Daucus carota L. seed against triton X-100 induced oxidative stress in mice. Scientific African. 8, e00429. https://doi.org/10.1016/j.sciaf.2020.e00429

Tijjani, H., Egbuna, C., Luka, C.D., 2018. Biosynthesis of Phytochemicals. Fundamentals, Modern Techniques, and Applications. 1, 37–78. https://doi.org/10.1201/9780429426223-2

Tijjani, H., Mohammed, A., Ahmed, F., Yahaya, H., Zakka, N., 2020. In vitro antioxidant activity-guided fractionation of Daucus carota L. seed extract. Proceedings of the Nigerian Academy of Science. 13(2), 74–85.

Tijjani, H., Mohammed, A., Muktar, S., Musa, S., Abubakar, Y., Adegunloye, A.P., Ishola, A.A., Joel, E.B., Luka, C.D., Alhassan, A.J., 2020. Antioxidant and antihyperlipidemic effects of aqueous seed extract of Daucus carota L. in triton ×100-induced hyperlipidemic mice. Journal of Applied Biology and Biotechnology. 8(1), 76–83. https://doi.org/10.7324/JABB.2020.80113

Topal, M., Gocer, H., Topal, F., Kalin, P., Köse, L.P., Gülçin, I., Cakmak, K.C., Kucuk, M., Durmaz, L., Gören, A.C., Alwasel, S.H., 2015. Antioxidant, antiradical, and anticholinergic properties of cynarin purified from the Illyrian thistle (Onopordumillyricum L.). Journal of Enzyme Inhibition and Medicinal Chemistry. 20, 1–10. https://doi.org/10.3109/14756366.2015.1018244

Tzung-Hsun, Tsai, P.-J., Su-Chen, Ho., 2005. Antioxidant and anti-inflammatory activities of several commonly used spices. Journal of Food Science. 70, 93–100. https://doi.org/10.1111/j.1365-2621.2005.tb09028.x

Umukoro, S., Ashorobi, R.B., 2005. Effect of Aframomum melegueta seed extract on castor oil-induced diarrhea. Pharmaceutical Biology. 43(4), 330–333. https://doi.org/10.1080/13880200590951748

Venkatesan, N., Thiyagarajan, V., Narayanan, S., Arul, A., Raja, S., Kumar, S.G.V., Rajarajan, T., Perianayagam, J.B., 2005. Antidiarrheal potential of Asparagus racemous wild root extracts in laboratoire animals. J Pharm Pharmaceut Sci. 8(1), 39–45.

Wang, S.Y., Huang, W.C., Liu, C.C., Wang, M.F., Ho, C.S., Huang, W.P., Hou, C.C., Chuang, H.L., Huang, C.C., 2012. Pumpkin (Cucurbita moschata) fruit extract improves physical fatigue and exercise performance in mice. Molecules. 17(10), 11864. https://doi.org/10.3390/molecules171011864

Whyte, L.A., Jenkins, H.R., 2012. Pathophysiology of diarrhea. Paediatrics and Child Health. 22(10), 443–447. https://doi.org/10.1016/j.paed.2012.05.006

Xu, D.P., Li, Y., Meng, X., Zhou, T., Zhou, Y., Zheng, J., Zhang, J.J., Li, H.B., 2017. Natural Antioxidants In Foods And Medicinal Plants: Extraction, Assessment And Resources. International Journal of Molecular Sciences. 18, 96–96. https://doi.org/10.3390/ijms18010096