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Research Article

Polyphenol-rich Extract of *Digitaria exilis* (Kippist) Grain Lowers Gastrointestinal Dysmotility and Enhanced Colonic Peristalsis in Rifaximin-induced Constipated Rat

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ABSTRACT

Digitaria exilis grains rich in polyphenol have been speculated among some traditional practitioners of Northern Nigeria to aid in treating constipation. Hence, this study aims at assessing the anti-constipation property of polyphenol-rich extract of *Digitaria exilis* grains (PREDEG) in rifaximin-induced constipated rat. Thirty (30) Wistar rats of both sexes (143.84 ± 2.62 g) were assigned into 6 categories, A to F, of 5 rats each. Category A (control) received 0.4 ml of saline. Constipations were induced in categories B to F by oral administration of rifaximin (2 mg/kg in saline for 48 h) and treated respectively with saline, glycerine (reference drug at 40 mg/kg), 50, 150 and 250 mg/kg of PREDEG (extracted via standard methods). All the treatments were given orally for 6 days using oral device. Rifaximin-induced constipation significantly ($p < 0.05$) decreases the feed and water intake, faecal quality, bodyweight and gastrointestinal flow proportion. All these alterations were attenuated dose-dependently, when co-treated with PREDEG and highest activity recorded at 250 mg/kg compared to reference drug. The data present polyphenol-rich extract of *D. exilis* grains as a potent anti-constipation agent and may act probably by lowering gastrointestinal dysmotility. This validates its traditional use in the treatment of constipation mostly in the Northern part of Nigeria.

Keywords: *Digitaria exilis, Constipation, Polyphenol, Purgative, Gastrointestinal dysmotility, Rifaximin*

INTRODUCTION

Constipation is defined as irregular passage of stool or difficulty in removal of stool (Bharucha *et al*., 2013; Felman and Stacy-Sampson, 2019). Severe constipation is among the frequent alimentary issues, affecting 20% of matured persons and 35% of persons higher than age 70 (Mugie *et al*., 2011; Chumpitazi *et al*., 2016). Digestive disorder constitute several features such as inability of discharging solid waste, strenuous stool release, excreting fewer faeces than normal as well as coagulated, crispy, or stony stools (Kim *et al*., 2021). Complications of intense digestive tract disorder are celiac hemorrhage after stretching; duodenal opening, which is a little tear close to the gut (Kellerman and Rakel, 2019); indicative lump which are swollen bloated, blistered arterial vessels in the celiac; excreta embedment, which arise when crispy body waste fester and accumulate in the celiac and gut, possibly leading to involuntary hindrance as well as low standard of life and neuronal discomfort (Kellerman and Rakel, 2019; Day, 2020). It is caused by lack of fiber in the diet (El-Salhy *et al*., 2017), physical inactivity, irritable bowel syndrome, aging, changes in routine, overuse of laxatives, not drinking enough water, colorectal problems and selected medications that can increases the risk such as opioid pain relief drugs, tricyclic antidepressants, certain anticonvulsants, calcium channel blockers, antacids that contain aluminum and calcium, iron supplements (Andrews and Storr, 2011; Ferri, 2019; Ohkusa *et al.,* 2019).

Digestive tract disorder can be tackled via non-pharmacologic strategies and medicative means. The familiar non-pharmacologic regime are dietetic (fiber and proper liquid ingestion), nutritive pattern advancement, and incision (Ikarashi *et al*., 2011; Lee *et al*., 2020). Pharmacologic approaches in the reference medication of alimentary canal disorder are medications like purgatives, duodenal secretants, depressant competitor and serotonin receptive combater (Lee *et al*., 2014; Nee *et al*., 2018). However, previous investigations have revealed that about 47% of sufferers are dissatisfied with their current anti-constipation medications accounting for the inadequacies including potency connected (less useful and contradictory outcomes), harmful feelings and financial consideration (Mounsey *et al*., 2015; Wamuyu *et al*., 2020). Medicinal plants have long been utilized in traditional medicine, worldwide ethno-medicine and in conventional drug production for the treatment and management of several experimental and clinical disorders (Belayneh *et al*., 2012). The dissatisfaction by sufferers is an issue of concern and the need to find alternative treatment choice in medicinal plants became crucial. Consequently, there are a few substitute medicative choices to cure constipative disorder globally. Among the local and commonly used herbs in northern Nigeria for the treatment of constipation is *Digitaria exilis*.

Digitaria exilis (family: Poaceae) is commonly known as Hungry rice in English. In Nigeria, *D. exilis* grain is locally known as *Acha* (Hausa) and *Suuru* (Yoruba) (Morales-Payan *et al*., 2002). It is a yearly, flower-patterned plant that is loosely-growing, vertical, slim and smooth stalk and grows up to 70 cm in height (Adoukonou-Sagbadja, 2010). Nationally, it is extensively cultured in the calm borders of the Plateau state including other states like Taraba, Kaduna, Niger, Jigawa and Kebbi where it is involved in the production of lettuce, cabbage, soup, yam meal, cake or other wheat products. Published works on *D. exilis* grains include anti-stroke activity (Taylor *et al*., 2006), antidiabetic role (Adams and Yakubu, 2020), physiochemical, lipid and amine, chemical component and oxygen inhibitor status (Glew *et al*., 2013), microstructure and nutritional component (Ballogou *et al*., 2013), postprandial proportion and postprandial load of *D. exilis* in normal and diseased models (Alegbejo *et al*., 2011), mutilation of salivary ptyalin from *D. exilis* (Egwim and Oloyede, 2008). Olagunju *et al*. (2018) have emphasized the 70:30 proportion augmentation of *D. exilis* flour with *Cajanus cajan* wheat which displayed the greatest repressive role opposed to salivary ptyalin and intestinal maltase and thus effective as nutritive diet in the healing of high blood sugar and as prophylaxis for related degenerative disorders. However, the dearth of empirical information to confirm the acclaimed laxative abilities of *D. exilis* in the treatment of constipation necessitated the current investigation. Herein, this study puts forward the anti-constipative capacity of polyphenol-rich extract of *D. exilis* grain in rifaximin-induced constipation in rats.

MATERIALS AND METHODS

Chemicals and reagents

Rifaximin was obtained from Pharmaffiliates, Haryana, India. Glycerine from Afrik Pharmaceuticals, Awo-Omamma, Nigeria. All other consumables, which are of diagnostic quality, are products of Afrab-Chem Ltd, Isolo Industrial Estate, Lagos and packaged using relevant sterile glassware and refined water. These products are thereafter stored in clean reagent bottles until they are being used.

Plant acquisition and identification

The plant acquired from herb users at a forest merchant in Kuje, Abuja was identified and confirmed at the Plant Biology Unit, University of Ilorin, where a Plant Identifier (I.U.V. No. 007) was assigned in the Herbarium.

Experimental animals and ethical guideline

White rats (*Rattus norvegicus*) of both sexes weighing 143.84 ± 2.62 g were acquired within the premises of the Zoological Facility of the Nigerian Institute for Animal Management, Jos, Nigeria. The study was carried out in compliance with the guidelines for Veterinary and Experimental Model Management (NIH Publication, No. 85-23), followed by the National Research Council's Guide for the Care and Use of Laboratory Animals.

Composition of plant material and derivation of polyphenol

Grains of *D. exilis* were scorched under shade at 20 ^{0}C until a constant density was derived. The dehydrated grains were squashed to granulated structure using an automated vitamizer (Kenwood Food Processor, model ZJM811RD, UK). The granulated sample (200 g) was drenched in 2 liter of n-hexane to discharge it of lipophilic molecules (defatted). The debris derived was evaporated and singly liquefied in 70% watery methanol and 70% aqua acetone separately for 20 hours with infrequent quivering to extricate the polyphenols as opined by Brglez-Mojzer *et al*. (2016). Both extracts were joined and sieved firstly using a percolated cloth followed by Whatman No. 1 sieving material. The product derived was evaporated at 35 ^{0}C with a water vaporizer to produce 12.25%. An estimated quantity of the vaporizer product was mixed with refine water to generate dossal levels (50, 150 and 250 mg/kg body mass). The doses employed in this investigation were obtained following a preparatory study conducted on the rats. The dossal levels of 50 and 150 is equivalent, individually, to "a filch" and "a spoon" of the plant powder often held to be ingested as therapy by a matured 68 kg man. The 250 mg/kg body weight dose which is five-times of the lowest dose was used to ascertain the occurrence of 'misuse' by the consumers.

$$\text{Percent produce} = \frac{\text{Density of extricate (g)}}{\text{Density of granulated plant (g)}} \times 100$$

Estimation of polyphenol

The entire phenolic quantity in the grain extract was estimated by the Folin-Ciocalteu guidelines of Deori *et al.* (2014). Concisely, 0.45 ml of the extract was added to Folin-Ciocalteu solution (2.0 ml, diluted 9 times) and heated for 5 minutes at 24 ^{0}C followed by introducing $NaCO_3$ (3 ml, 7.0% w/v). The solution was made to fully saturate for 20 minutes at 24 ^{0}C and read at 680 nm spectrophotometrically. The entire amount of phenolic was computed as a gallic acid proportionate with relevant phenol curve of gallic acid stock mixture and presented as mg gallic acid /g of extract.

Flavonoid constituent

The whole flavonoid present in the grain was assessed by the style of Deori *et al.* (2014). Briefly, 1 ml of the extract was added to 1 ml of $AlCl_3$ prepared in 3% methanolic solution. It was thereafter read spectrophotometrically after 5 minutes at 450 nm. Quercetin was used to compare values obtained and is represented as mg quercetin/g scorched density of the extract.

Animal categorization and extract intake

Thirty (30) rats of both sexes (143.84 ± 2.62 g) were assigned into 6 categories, A to F of 5 rats each. Category A (control) received 0.4 ml of saline. Constipations were induced in categories B to F by oral administration of rifaximin (2 mg/kg in saline for 48 h) (Bustos *et al*., 1991) and treated respectively with saline, glycerine (reference drug at 40 mg/kg), 50, 150 and 250 mg/kg of polyphenol-rich extract of *D. exilis* grains (PREDEG, extracted via standard methods). All treatments were given orally for 6 days using oral pharyngeal device. The feed and water intake, faecal quality, body weight and gastrointestinal tract flow proportion were recorded at the end of the study.

Total number, dry weight and water content of faecal pellet

The pelletized faeces of every single animal was picked daily at the 08:00 hour while the investigation last. The quantity, density and fluid content of the pelletized faeces were ascertained. The fluid content was estimated as the disparity amid the moist and dehydrated weight of the faeces (Yakubu *et al*., 2011; Rtibi *et al*., 2017).

Gastrointestinal tract flow proportion

The digestive tract proportion was computed using the guideline of Nagakura *et al.* (1996) with little methodological improvement. Briefly, on the 8th day, 1 ml of orcein (2 g mixed in 40 ml of 1% carboxymethylcellulose) instead of carmine used by Nagakura *et al.* (1996) was injected by oral means into animals. One hour after placing drops of orcein, the animals were gently dissected when the small intestines expunged using the guideline of Guarize *et al.* (2012). The interval the orcein had travelled along and the whole stretch of the duodenum were recorded. The digestive canal proportion was presented as the percentage of the interval travelled by orcein in relative to the entire width of the small intestine.

$$\text{Digestive tract flow proportion (\%)} = \frac{\text{Interval moved by orcein}}{\text{Entire stretch of the duodenum}} \times 100$$

Data analysis

Results were presented as the mean ± standard error mean (SEM) of five components. A one-sided estimation of variation together with the Turkey's Multiple Limit Estimate was used to determine the analytical weightiness of distinction in biomarkers across groups using SPSS version 18.0 Spreadsheet. The degree of substantive disparity was taken at $p < 0.05$.

RESULTS

Determination of polyphenol content

The assessment of polyphenol constituent in grain extract of *D. exilis* showed that it is high in phenolics and flavonoids; the phenolic and flavonoid components were 32.52 ± 1.52 mg gallic acid equivalent / g dry extract and 36.73 ± 1.95 mg quercetin equivalent/g dry extract, respectively (Table 1).

Table 1. Phenolic and Flavonoid Components in *D. exilis* Grain Extract

Composition	Concentration per g dry
Phenolics	32.52 ± 1.52 mg gallic acid equivalent
Flavonoids	36.73 ± 1.95 mg quercetin equivalent

Values were expressed as mean ± SEM (n = 3)

Impact of rifaximin on some markers of constipation in rats

Treatment without rifaximin substantively ($p < 0.05$) dropped the fluid ingestion, quantity, water absorbed, and density of the stool pieces when liken with the distilled water treated control animals (Table 2). However, the feed consumption by the rifaximin treated constipated animals was notably ($p < 0.05$) lowered when matched with the refined aqua treated reference rats (Table 2).

Table 2. Influence of Rifaximin on a Few Markers of Constipation in Rats

Markers	Reference	Constipated rats
Food consumption (g)	92.24±2.05[a]	91.64±0.16[a]
Fluid ingestion (g)	125.84±1.29[a]	106.39±0.09[b]
Quantity of stool pieces	316.57±4.73[a]	269.84±2.78[b]
Fluid content of stool pieces (g)	9.72±0.02[a]	4.35±0.01[b]
Weight of faecal pellet (g)	56.74±1.43[a]	41.93±0.87[b]

Values were expressed as mean ± SEM (n = 5). Values with different letters (a, b) across the row are significant at $p < 0.05$

Impact of polyphenol-rich grain extract of *Digitaria exilis* on some markers of constipation in rats

The extract at all the doses as well as the glycerine did not sufficiently *($p > 0.05$)* change the feed consumption rate of the animals (Table 3). Water intake dropped glaringly *($p < 0.05$)* in the constipated untreated animals. On the other hand, the extract at 50, 150, 250 mg/kg body weight as well as the glycerine did not substantively *($p > 0.05$)* affect the fluid intake of the animals (Table 3). When liken with the constipated untreated rats, the extract at all doses notably *($p < 0.05$)* increased the quantity of faecal pellet of the animals. This increment, which matched well with the glycerine treated constipated animals, was still lowered when related to the distilled water treated animals (Table 3). Furthermore, the extract at all doses increased the water content in the stool pellets of the animals in a dose-dependent fashion. These increases by the extract juxtaposed with glycerine and non-constipated distilled water treated animals. The similar rise in the density of the stool pieces by the extract and glycerine did not match *($p > 0.05$)* well with the non-constipated sublimed water treated rats (Table 3). While the body weight was glaringly *($p < 0.05$)* raised in the constipated untreated animals when matched with the non-constipated distilled water treated animals, the extract and glycerine treated animals did not sufficiently *($p > 0.05$)* change the weight of the animals (Table 3).

Table 3. Influence of Polyphenol-rich Grain Extract of *Digitaria exilis* on Some Markers of Constipation in Rats

				Constipated + *D. exilis* (mg/kg body weight)		
Parameters	Control	Constipated	Glycerine	50	150	250
Feed intake (g)	75.24±1.63[a]	62.19±0.96[b]	75.82±0.32[a]	77.56±1.03[a]	78.61±0.97[a]	76.36±1.25[a]
Water intake (ml)	123.16±1.95[a]	104.35±0.84[b]	122.36±1.52[a]	125.49±1.77[c]	124.89±1.96[c]	125.22±1.08[c]
Number of faecal pellet	328.51±3.15[a]	243.73±2.65[b]	307.41±3.02[c]	281.33±1.82[d]	279.14±1.08[d]	305.15±2.96[c]
Water content of faecal pellet (g)	12.36±0.12[a]	8.00±0.13[b]	11.22±0.04[a]	12.85±0.16[a]	14.02±0.27[a]	13.47±0.03[a]
Weight of faecal pellet (g)	38.46±0.74[a]	23.84±0.04[b]	30.72±0.25[c]	35.91±0.15[d]	29.36±0.93[c]	32.08±0.16[c]
Body weight gain (g)	11.32±0.05[a]	19.25±0.12[b]	12.87±0.04[a]	14.02±0.25[a]	13.08±0.16[a]	12.06±0.02[a]

Values were expressed as mean ± SEM (n = 5). Values with different letters (a, b, c, d) across the row are significant at $p < 0.05$

Influence of orcein on gastrointestinal tract flow of models

The extract remarkably ($p < 0.05$) heightened the computed gastrointestinal (GIT) range (Table 4). While the values at 50 mg/kg body weight of the extract matched suitably ($p > 0.05$) with the non-constipated refined water injected control rats, the constipated animals given 250 mg/kg body weight of the extract heightened the GIT proportion in a fashion similar *($p > 0.05$)* to those of the glycerine treated rats. In contrast, the GIT ratio was lessened in the constipated models (Table 4).

Table 4. Influence of Orcein on Gastrointestinal Tract Flow of Rats

Category of models	Gastrointestinal transit ratio
Distilled water treated control model	28.64 ± 0.56[a]
Distilled water treated constipated animals	12.52 ± 0.28[b]
Glycerine treated constipated model	36.41 ± 0.63[c]
Constipated + 50 mg/kg body weight	55.03 ± 1.05[d]
Constipated + 150 mg/kg body weight	43.15 ± 0.74[e]
Constipated + 250 mg/kg body weight	62.85 ± 1.45[f]

Values were expressed as mean ± SEM (n = 3)

DISCUSSION

The present global interest in natural products from both pharmaceutical outlets and herbal users is rapidly rising owing to their safety and healing capacities. The medicinal uses displayed by plants are due to the abundance of phytochemicals and some polyphenolic fractions (Adams and Eze, 2022). Flavonoids and phenolics constitute the main class of polyphenols present in flora including grains and spices. Polyphenols possess pathogen eliminating and therapeutic advantage mainly due to their capacity to damage oxygen-mediated interactions in the internal environment. Hence, they perform nutraceutic role for a number of gastrointestinal stress implicated diseases like constipation and other gastrointestinal dysfunction (Koudoufio *et al*., 2020). It has been affirmed that they improve intestinal motility (Alina, 2019), enhance colonic peristalsis (Caban and Lewandowska, 2022) and facilitate stool softening (Veronique *et al*., 2021) as well as reduction in the incidence of 'complexness' linked with gastrointestinal dysfunction and irritable bowel syndrome (IBS) (Roudsari *et al*., 2019).

Plants have been used over decades as a source of both conventional and unconventional medications against several ailments including constipation. Greater proportion of the Nigerians rely on herbs for the cure of digestive tract disorder since the synthetic purgatives are becoming increasingly exorbitant, inaccessible, delayed activity with its unpleasant harmful impact including retching, farting, unusual contraction, dysentery, bowel disruption and colon and rectal malignancy (Li *et al*., 2021). In this work, we examined the anti-constipation action of the polyphenol-rich grain extract of *D. exilis* as an alternative medication in the healing of constipation as evidenced by its ability to lower gastrointestinal dysmotility relative to glycerine (a reference anti-constipated drug).

Rifaximin, an opioid synthetic cyclopentimine derivative, is commonly used to instigate digestive tract disorder in experimental models. It causes alimentary obstruction in models by inhibiting intestinal fluid release (Zhuang *et al*., 2019) and rectal motility and consequently, the free-flow and/or passage of metabolite down the bowel (Zhuang *et al*., 2019). This repressive action stretches bodily stool discharge period and thus celiac phenobarbital flow (Rtibi *et al*., 2017). Rifaximin-induced constipation is thus used as a platform for induction of intermittent constipation (Krause *et al*., 2011). Therefore, the drop in quantity, mass and aqua levels of stool pieces after injecting the animals with rifaximin suggests inhibitory effect on intestinal water secretion which prolonged the time needed to evacuate the stools. This might however be a consequence of reduction in the intake of water in the present investigation. All these indicate that constipation was induced in the rat model by the rifaximin and further corroborates the use of rifaximin as an inducer of constipation (Pimentel *et al*., 2011). Similar drop in the amount, mass and fluid constituent of stool pellets by rifaximin have been emphasized in successive investigations by Rtibi *et al*. (2017), Li *et al*. (2021) and Zhan *et al*. (2021). Interestingly, the lowered state of water intake had no substantive impact on the appetite of the model for food as the values obtained were not sufficiently different from themselves.

Glycerine, an oral hyperosmotic laxative, heightens intestinal locomotion by stimulating the colonic nerves (Sardi *et al*., 2018). The polyphenol-rich extract generated close-ranged effect with those of glycerine and other stool biomarkers. Therefore, the rise in the quantity, fluid and mass component of stool pellets suggests that the extract was effective in shifting the balance between the removal of fluid from the gastro-enteric cavity via a direct active transport mechanism (Anabrees *et al*., 2015) and the discharge of fluid into the alveolus by dinoprostone-reliant strategy to favour the enhancement of motility of the faeces through the bowel (Farinde, 2020). This "lubrication effect" might have resulted in increased defecation in the constipated models treated with the polyphenol-rich extract. The observed gastrointestinal flow in the rifaximin-injected clogged animal by the extract confers anti-constipation power on the polyphenol-rich grain extract of *D. exilis*. The improved feed and fluid ingestion in the constipated animal treated with the polyphenol-rich extract relative to glycerine (a standard reference drug) further buttress the effectiveness of the extract as a purgative. It is also important to emphasize that the extract could not lead to morbid obesity whereas the constipated rats that received distilled water gained weight probably due to aggregated pelletized stool in their system (Jabri *et al*., 2017; Sardi *et al*., 2018) which might have hindered the colonic flow. Enhanced bowel flow and increased electrolyte as well as water transportation in the colon with inversion of the physiological pattern are the most crucial modes of action of polyphenol (Anabrees *et al*., 2015; Jabri *et al*., 2017; Sardi *et al*., 2018; Kim *et al*., 2018; Farinde, 2020; Zhan *et al*., 2021). Therefore, the presence of polyphenol in the extract of *D. exilis* grain may account for the anti-constipation action displayed by the plant. However, there is possibility of synergistic effect with other phytochemicals present in the extract.

The movement along the whole digestive canal reflects a general alimentary tract flow process. Furthermore, measurement of rectal flow period is important in constipation, intestinal swell and severe alimentary canal disorder as it provides valuable details on celiac movement and enables the confirmation of abdominal flow distortion. It also helps to detect the extent of the disorder as well as drug reaction (Han *et al*., 2017). Also, the rise in alimentary tract proportion by the polyphenol-rich extract, suggests facilitated digestive tube flow and rectal function in the animal. The extract has the capacity to increase discharge and lowers gastrointestinal dysmotility (Aslam and Janbaz, 2019).

CONCLUSION

The data present polyphenol-rich extract of *D. exilis* grains as a potent anti-constipation agent and may act probably by lowering gastrointestinal dysmotility. This validates its traditional use in the treatment of constipation-related disease mostly in the Northern part of Nigeria. Further experimental investigations to obtain the functional bioactive component(s) in the polyphenol grain extract are required.

AUTHORS' CONTRIBUTIONS

Conceptualization and design of the study was by **MDA**. Acquisition of data was carried out by **MDA** and **OAS** while analysis and interpretation of data was by **MDA** and **TKM**. Authors **MDA**, **TKM** and **OAS** drafted and revised the manuscript and gave approval for its publication.

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CONFLICT OF INTEREST

The authors no competing interest.

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REFERENCES

Adams, D. M., and Yakubu, M. T. (2020). Aqueous extract of *Digitaria exilis* grains ameliorate diabetes in streptozotocin-induced diabetic male Wistar rats. *Journal of Ethnopharmacology*, *249*, 112383.

Adams, M. D., and Eze, E. D. (2022). *Borassus aethiopum* (Mart.) ethanol fruit extract reverses alloxan-treatment alterations in experimental animals. *Mediterranean Journal of Nutrition and Metabolism*, *15*, 429–445.

Adoukonou-Sagbadja, A. H. (2010). Genetic characterization of traditional fonio millets (*Digitaria exilis*, *D. iburua* Stapf) landraces from West-Africa: implications for conservation and breeding. PhD thesis submitted by M.Sc Hubert Adoukonou-Sagbadja to Justus-Liebig University, Germany from University of Abomey-Calavi, Giessen, Cotonu, Benin Republic.pp. 107 BP 526, 2010.

Alegbejo, J. O., Ameh, D. A., Ogala, W. M., and Ibrahim, S. (2011). Glycaemic index and load of Acha (Fonio) in healthy and diabetic subjects. *Journal of Pure and Applied Microbiology*, *5*(1), 117–122.

Alina, P. (2019). What Are Polyphenols? Types, benefits, and food sources. biomolecules as basis of nutrients. *Molecules*, *67*(5), 163-169.

Anabrees, J., Shah, V. S., Al-Osaimi, A., and Al-Faleh, K. (2015). Glycerine laxatives for prevention or treatment of feeding intolerance in very low birth weight infants. *Cochrane Database Systematic Review*, 9, 1-22.

Andrews, C. N., and Storr, M. (2011). The pathophysiology of chronic constipation. *Canadian Journal of Gastroenterology*, *25*(suppl B), 16B-21B.

Aslam, N., and Janbaz, K. H. (2019). Studies on antidiarrheal and laxative activities of aqueous-ethanol extract of *Asphodelus tenuifolius* and underlying mechanisms. *BMC Complementary and Alternative Medicine*, *19*(1), 307.

Ballogou, V. Y., Soumanou, M. M., Toukourou, F., and Hounhouigan, J. D. (2013). Structure and nutritional composition of Fonio (*Digitaria exilis*) grains: a review. *International Research Journal of Biological Sciences*, *2*(1), 73–79.

Belayneh, A., Asfaw, Z., Demissew, S., and Bussa, N. F. (2012). Medicinal plants potential and use by pastoral and agro-pastoral communities in Erer Valley of Babile Wereda, Eastern Ethiopia. *Journal of Ethnobiology and Ethnomed*icine, *8*(1), 1-11.

Bharucha, A. E., Pemberton, J. H., and Locke, G. R. (2013). American Gastroenterological Association technical review on constipation. *Gastroenterology*, *144*, 218-238.

Brglez-Mojzer, E., Knez-Hrnčič, M., Škerget, M., Knez, Ž., and Bren, U. (2016). Polyphenols: extraction methods, antioxidative action, bioavailability and anticarcinogenic effects. *Molecules*, *21*(7), 901.

Bustos, D., Ogwa, K., Pons, S., Soriano, E., Bandi, J. C., Bustos, T., and Fernandez, L. (1991). Effect of loperamide and bisacodyl on intestinal transit time, fecal weight and short chain fatty acid excretion in rat. *Acta Gastroenterol Latinoam*, *12*, 3-9.

Caban, M., and Lewandowska, U. (2022). Polyphenols and the potential mechanisms of their therapeutic benefits against inflammatory bowel diseases. *Journal of Functional Foods*, *95*, 105181.

Chumpitazi, C. E., Henkel, E. B., Valdez, K. L., Bruno, P., and Chumpitazi, B. P. (2016). Soap suds enemas are efficacious and safe for treating fecal impaction in children with abdominal pain. *Journal of Pediatric Gastroenterology and Nutrition*, *63*(1), 15-8.

Day, M. R. (2020). Constipation: epidemiology, assessment and treatment options. Promoting continence and management of incontinence conference. Published April 19, 2017. Accessed April 30, 2020. http://www.muh.ie/images/CNE/ConstipationEpidemiology.pdf

Deori, M., Boruah, D.C., Devi, D., and Devi, R. (2014). Antioxidant and antigenotoxic effects of pupae of the muga silk worm *Antheraea assamensis*. *Food Biosciences*, *5*, 108-114.

Egwim, E. C., and Oloyede, O. B. (2008). Immobilization of α-amylase from Acha (*Digitaria exilis*) on different cellulose fibre materials. *Asian Journal of Biochemistry*, *3*(3), 169–175.

El-Salhy, M., Ystad, S. O., Mazzawi, T., and Gundersen, D. (2017). Dietary fiber in irritable bowel syndrome. *International Journal of Molecular Medicine*, *40*(3), 607–613.

Farinde, A. (2020). Laxatives, stool softeners, and prokinetic agents. *Drugs and Disorders*, *34*(5), 121-135.

Felman, A., and Stacy-Sampson, D. O. (2019). What to know about constipation? 5th Edition. Health-line Media. p. 342-349, 2019.

Ferri, F. F. (2019). Constipation. In: Ferri's Clinical Advisor 2019. 1st Edition. Philadelphia, Pa.: Elsevier; 2019. https://www.clinicalkey.com. Accessed June 4, 2019.

Glew, R. H., Laabes, E. P., Presley, J. M., Schulze, J., Andrews, R., Wang, Y., Chang, Y., and Chuang, L. (2013). Fatty acid, amino acid, mineral and antioxidant contents of Acha (*Digitaria exilis*) grown on the Jos Plateau, Nigeria. *International Journal of Nutrition and Metabolism*, *5*(1), 1–8.

Guarize, L., Costa, J. C., Dutra, L. B., Mendes, R. F., Lima, I. V., and Scio, E. (2012). Anti-inflammatory, laxative and intestinal motility effects of *Senna macranthera* leaves. *Natural Product Research*, 26, 331-334.

Han, S. H., Park, K., Kim, E. Y., Ahn, S. H., Lee, H. S., and Suh, H. J. (2017). Cactus (*Opuntia humifusa*) water extract ameliorates loperamide-induced constipation in rats. *BMC Complementary and Alternative Medicine*, *17*(1), 49.

Ikarashi, N., Mochiduki, T., and Takasaki, A. (2011). A mechanism by which the osmotic laxative magnesium sulphate increases the intestinal aquaporin 3 expression in HT-29 cells. *Life Sciences*, *88*, 194-200.

Jabri, M. A., Wannes, D., Hajji, N., Sakly, M., Marzouki, L., and Sebai, H. (2017). Role of laxative and antioxidant properties of *Malva sylvestris* leaves in constipation treatment. *Biomedicine and Pharmacotherapy*, *89*, 29–35.

Kellerman, R. D., and Rakel, D. (2019). Constipation. In: Conn's Current Therapy 2019. Philadelphia, Pa.: Elsevier; 2019. https://www.clinicalkey.com. Accessed June 4, 2019.

Krause, R., Zollner-Schwetz, I., and Valentin, T. (2011). Rifaximin for irritable bowel syndrome without constipation. *The New England Journal of Medicine*, *364*(15), 1467-1468.

Kim, J. E., Choi, Y. J., Lee, S. J., Gong, J. E., Jin, Y. J., Park, S. H., ... and Hwang, D. Y. (2021). Laxative effects of phlorotannins derived from Ecklonia cava on loperamide-induced constipation in SD rats. *Molecules*, *26*(23), 7209.

Kim, J. E., Lee, M. R., Park, J. J., Choi, J. Y., Song, B. R., Son, H. J., and Hwang, D. Y. (2018). Quercetin promotes gastrointestinal motility and mucin secretion in loperamide-induced constipation of SD rats through regulation of the mAChRs downstream signal. *Pharmaceutical Biology*, *56*(1), 309–317.

Koudoufio, M., Desjardins, Y., Felman, F., Spahis, S., Delvin, E., and Levy, S. (2020). Insight into polyphenol and gut microbiota crosstalk: are their metabolites the key to understand protective effects against metabolic disorders? *Antioxidants*, *9*(10), 982.

Lee, H., Choi, E., Park, S., and Lee, J. (2020). Laxative and antioxidant effects of Ramie (*Boehmeria nivea* L.) leaf extract in experimental constipated rats. *Food Science and Nutrition*, 8, 3389–3401.

Lee, M. J., Choi, S., and Im, W. (2014). 5-HT4 receptor agonists in the treatment of gastrointestinal motility disorders: current status and perspective. *International Journal of Gastroenterology and Disorder Therapy*, *1*, 1-8.

Li, T., Hu, M., Jiang, C., Zhang, D., Gao, M., Xia, J., Miao, M., Shi, G., Li, H., Zhang, J., and Yin, Z. (2021). Laxative effect and mechanism of Tiantian Capsule on loperamide-induced constipation in rats. *Journal of Ethnopharmacology*, *266*, 113411.

Morales-Payan, J. P., Richard, O. J., Julio, C. T., and Francisco, T. S. (2002). *Digitaria exilis* as a crop in the Dominican Republic. In: Janick, J., Whipkey, A. (Eds.), Supplement to: Trends in New Crops and New Uses. ASHS Press, Alexandria, VA. 2002.

Mounsey, A., Raleigh, M., and Wilson, A. (2015). Management of constipation in older adults. *American Family Physician*, *92*, 500-504.

Mugie, S. M., Benninga, M. A., and Di-Lorenzo, C. (2011). Epidemiology of constipation in children and adults: a systematic review. *Best Practice in Research and Clinical Gastroenterology*, *25*, 3-18.

Nagakura, Y., Naitoh, Y., Kamato, T., Yamano, M., and Miyata, K. (1996). Compounds processing 5-HT3 receptor antagonistic activity inhibit intestinal propulsion in mice. *European Journal of Pharmacology*, 311, 67-72.

Nee, J., Zakari, M., and Sugarman, M. A. (2018). Efficacy of treatments for opioid-induced constipation: systematic review and meta-analysis. *Clinical Gastroenterology and Hepatology*, 16, 1569-1584.

Ohkusa, T., Koido, S., Nishikawa, Y., and Sato, N. (2019). Gut microbiota and chronic constipation: a review and update. *Frontiers in Medicine*, *6*, 19.

Olagunju, A. I., Omoba, O. S., Enujiugha, V. N., and Aluko, R. E. (2018). Development of value added nutritious crackers with high antidiabetic properties from blends of Acha *(Digitaria exilis) and blanched Pigeon pea (Cajanus cajan). Food Science and Nutrition*, 6, 1791–1802.

Pimentel, M., Lembo, A., Chey, W. D., Zakko, S., Ringel, Y., Yu, J., ... and Forbes, W. P. (2011). Rifaximin therapy for patients with irritable bowel syndrome without constipation. *New England Journal of Medicine*, *364*(1), 22-32.

Roudsari, N. M., Lashgari, N. A., Momtaz, S., Farzaei, M. H., Marques, A. M., and Abdolghaffari, A. H. (2019). Natural polyphenols for the prevention of irritable bowel syndrome: Molecular mechanisms and targets; a comprehensive review. *DARU Journal of Pharmaceutical Sciences*, *27*, 755-780.

Rtibi, K., Selmi, S., Grami, D., Armi, M., Eto, B., El-benna, J., and Marzouki, L. (2017). Chemical constituents and pharmacological actions of carobpods and leaves (*Ceratonia siliqua* L.) on the gastrointestinal tract: A review. *Biomedicine and Pharmacotherapy*, *93*, 522–528.

Sardi, C., Garetto, S., Capone, L., Galbiati, V., Racchi, M., Govoni, S., ... and Lucci, J. (2018). Experimental paradigm for the assessment of the non-pharmacological mechanism of action in medical device classification: The example of glycerine as laxative. *Frontiers in Pharmacology*, *9*, 1410.

Taylor, J. R. N., Schober, T. J., and Bean, S. R. (2006). Novel food and non-food uses for sorghum and millets. *Journal of Cereal Science*, *44*, 252–271.

Veronique, T., Wing, Y. M., and Christian, D. (2021). Seabuckthorn polyphenols: characterization, bioactivities and associated health benefits. *IntechOpen*, 34(2), 263 – 269.

Wamuyu, K. R., Machocho, A. K., and Wafula, A. W. (2020). Antimicrobial and phytochemical screening of *Lannea schweinfurthii* (Engl.) Engl. *Bioteknologi*, 17, 1-13.

Yakubu, M. T., Adams, D. M., Akanji, M. A., and Oladeji, A. T. (2011). Laxative activity of aqueous root extract of *Cnestis ferruginea* (Vahl Ex DC) in loperamide-induced constipated rats. *Nigerian Journal of Gastroenterology and Hepatology*, 3, 21-29.

Zhan, Y., Wen, Y., Zhang, L. L., Shen, X. L., Chen, X. H., Wu, X. H., and Tang, X. G. (2021). Paeoniflorin improved constipation in the loperamide-induced rat model via TGR5/TRPA1 signaling-mediated 5-hydroxytryptamine secretion. *Evidence-Based Complementary and Alternative Medicine*, *2021*.

Zhuang, Z., Chen, M., Niu, J., Qu, N., Ji, B., Duan, X., ... and Zhao, B. (2019). The manufacturing process of kiwifruit fruit powder with high dietary fiber and its laxative effect. *Molecules*, *24*(21), 3813.