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Anti-diarrheal Activity of Ethanolic Extract of Moringa oleifera in Castor Oil-induced Entropooling and Gastrointestinal Motility Studies

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KEYWORDS
Phytomedicine, *Moringa oleifera*, Castor Oil, Anti-diarrheal Activity, Enteropooling model, Gastro-intestinal transit model

ABSTRACT:

Introduction: Humans have been using natural products for thousands of years to care for a wide range of diseases. The world's largest community in developing countries nearly exclusively uses traditional remedies to manage a variety of diseases, including diarrhea. The passage of three or more loose or liquid stools in a day or more frequently than is typical for an individual is considered diarrhea. Mostly, it is categorized as acute or chronic according to the duration that the symptoms continue. In low-income nations, infections brought on by diarrhea have been considered a serious public health concern due to their elevated rates of morbidity and mortality.

Objectives: The current research study aimed to estimate the ant-diarrheal activity and safety profile of *Moringa oleifera* root extract in rats.

Methods: Castor oil-induced diarrhea, castor oil-induced enteropooling and intestinal aggregation models were used to evaluate the anti-diarrheal activity of the tested extract at doses of 100, 200, and 400 mg/kg.

Results: Preliminary phytochemical screening test of *Moringa oleifera* root extract contained preset alkaloids, saponins, flavonoids, tannins, phenols, terpenoids, and steroids. *Moringa oleifera* root extract did not cause any deaths with a single test dose of 2000 mg/kg during the first 24 hours and for the remaining 14 days. The severity of diarrhea was significantly reduced ($P < 0.001$) by the ethanolic extract by 47.65%, 56.23%, and 61.75%, respectively, while 33.37% inhibition was observed with the standard drug Atropine 3 mg/kg. The extract also significantly reduced ($P<0.001$) intestinal volume in oil-induced enteropooling.

Conclusions: It is concluded that both fractions contain biologically active ingredients active in anti-diarrheal action, while the methanolic fraction has better potential.

1. Introduction

The passage of three or more loose or liquid stools in a day or more frequently than is typical for an individual is considered diarrhea. Mostly, it is categorized as acute or chronic according to the duration that the symptoms continue [1]. In low-income nations, infections brought on by diarrhea have been considered a serious public health concern due to their elevated rates of morbidity and mortality. It accounts for over 15% of all child mortality under the age of five, or over 1600 deaths every day [2,3]. Africa and Southeast Asia account for over 80% of all pediatric diarrheal mortality [4]. Diarrhea in kids under 5 years old has been attributed to approximately 25% and 31% of the global diarrheal burden in Africa and Asia [5].

Humans have been using natural products for thousands of years to care for a wide range of diseases. The world's largest community in developing countries

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nearly exclusively uses traditional remedies to manage a variety of diseases, including diarrhea [6,7]. Biologically active molecules have been demonstrated to be abundant in medicinal plants, and many of these substances are utilized to generate lead compounds [8]. Approximately 25% of traditional medications are made entirely of botanical ingredients. The remaining ones are synthetic substitutes derived from model compounds derived from therapeutic plants [9,10]. For instance, "berberine" is made from the bark and root extracts of "Berberis aristata" and is regularly prescribed in modern pharmacopeia to treat diarrhea [11].

Other names for *Moringa oleifera* include drum stick tree and horse radish tree. The plant known as munga, or *Moringa oleifera*, is to sub-Himalayan regions of Afghanistan, Bangladesh, Pakistan, and India. It is a small, rapidly growing deciduous or evergreen tree. It typically reaches a height of 10 to 12 meters [12]. A significant and uncommon amalgamation of zeatin, quercetin, kaempferol, beta-sitosterol, and caffeoylguinic acid is found in munga plants [13,14]. Alkaloids, tannins, terpenoids, steroidal aglycones, and reducing sugars and flowers, among other components of the plant, are among the many significant phytoconstituents found in leaves, roots, bark, seeds, flowers, and adolescent pods. Essential amino acids found in plant leaves help develop strong, healthy bodies [12]. In addition to being a common food in these areas, munga is also distinguished for its health profit. It has been known to common people as "the miracle tree" because of its extraordinary healing powers for a wide range of illnesses, including some chronic conditions. Because of its many uses, several studies were conducted to separate bioactive components from different plant parts [15]. Since ancient times, the leaves of munga have been used in conventional medicine, particularly in the ayurveda system, to treat and prevent various diseases due to their potent detoxifying properties and high dietary value. Thus, herbal medicines also referred to as phytomedicine, have been used for centuries and are still considered reliable medical practices. For example, moringa has been used medicinally in many cultures worldwide to treat a wide range of conditions, including cholera, anemia, asthma, blackheads, bronchitis, catarrh, and skin infections [13,16,17]. In previous research, *Moringa oleifera* has anti-oxidant, anti-inflammatory, antipyretic, anti-hypertensive, anti-spasmodic, anti-tumor, anti-epileptic, anti-ulcer, anti-diabetic, diuretic and hepatoprotective activates [13, 18-21]. Additionally, munga has excellent cosmetic qualities; it has frequently been discovered to be utilized in a variety of healthcare products, such as conditioners and moisturizers for the body and hair [22].

2. Methods

2.1. Drugs, Chemicals & Reagents

Almost all of the chemicals and reagents used in this research were in their most pure form. Atropine (inj.), Petroleum ether, Chloroform, Ethanol, Potassium bromide, Iodine solution, Conc. HCL, potassium mercury iodide, NaOH, Acetic acid, Sulphuric acid, -naphthol, n-butanol, and n-hexane were among the organic and inorganic chemicals and reagents used for the extraction of dried leaves.

2.2. Experimental animals

Six to eight weeks old, healthy albino rats weighing about 120 and 180 grams were used in the research. The rats were kept in cages with comforters made of softwood shavings and chips in a light-and-dark cycle of 12 hours. They also had unlimited access to water and normal pellets at a temperature of 25 ± 2 ◦C. Before starting the primary experiment, they had seven days to get used to the lab setting.

2.3. Collection, identification Authentication of Plant Material:

We collected fresh *Moringa oleifera* roots from the Rudderpur and Moradabad local markets. The quality and freshness of the leaves determined the sample's selection. Prof. Ashok Kumar of the School of Sciences (Biological Science) at IFTM University in Moradabad, India, verified the sample (last number 2016/SOS/BOT/33). To get rid of dust and insects, pick up fresh leaves and give them ten thorough washings in clean water. Clean, fresh leaves are allowed to air dry at room temperature (37–40 °C). Using a fine grinder, the dried leaves are ground into a fine powder, which is further sieved to get rid of contaminants. The dried plant material will be ground into a powder and then run through a 20-ring filter. Materials in plant powder will

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be collected. Petroleum ether will be used as a solvent to extract the glowing powder, and the Soxhlet equipment will be used in sequence. By adding liquids to the melted water and allowing them to evaporate dry in a rotary vacuum evaporator, the discharges will be filtered and concentrated.

2.4. Preparation of extract

The roots were crushed into powder after being sun-dried to a powder. Using a Soxhlets apparatus, the root powder was deflated using pet ether and then extracted with ethanol. Filtered crude extract was dried at low pressure using a Test animals were given an appropriate dilution of ethanolic extract in distilled water.

2.5. Phytochemical Screening Test

A conventional qualitative method was used to assess whether active phytochemicals such as alkaloids, tannins, terpenoids, steroidal aglycones, and reducing sugars were present or absent [23].

2.6. Acute oral toxicity study:

As a result, five female mice weighing between 25 and 30 g were used. Before the animals were given the plant extract, they were all denied food for three hours. After administering a single dosage of 2000 mg/kg of the test sample, the mouse was closely observed for 4 hours, each 30 minutes, to look for any indications of toxicity and death within the first 24 hours. The extract was given to the next 3 mice in sequential order, each at an equivalent dose, based on the outcome of the first rat. After that, the rats were housed individually and watched for any indications of toxicity, including behavioral, autonomic, neurological, and physical abnormalities, every day for two weeks, followed by a 4-hour observation eriod separated by a 30-minute break [24].

2.7. Grouping of animals

The five groups of six rats each were created at random from the rats. Group I negative control group received distilled (10 ml/kg), even as groups II, III, and IV are designated as test groups received plant extract 100 mg/kg, 200 mg/kg, and 400 mg/kg respectively and group V positive control group received atropine (3 mg/kg) respectively.

2.8. Castor oil-induced diarrhea

After an 18-hour fast, thirty rats were separated into five individual groups have six rats in each group. Every treatment that was prescribed was administered orally. One hour following treatment, every rat was given 0.5 mL of castor oil to cause diarrhea. After that, each animal was put in its separate cage with a fresh, white paper ground. The flooring was changed every time the rodent urinated. Following that, throughout the 4-hour monitoring period, the rat's fecal output count, consistency, and time of beginning of diarrhea were all noted and compared with the negative control [25,26].

2.9. Castor oil-induced entropooling

The rats were dosed according to the before instructions and separated into five groups of 6 rats every group just before the experiment. After one hour, castor oil (0.5 ml) was administrated to every rat. The rats were administered castor oil for one hour, after which they were killed. Each rat's small intestine, from the pylorus to the cecum, was removed and weighed right away. The intestinal contents of every rat were then measured by milking, and the volume was noted. The difference between the small and empty intestines was then calculated when the gut was weighed again. [27,28].

2.10. Gastrointestinal motility test

Using charcoal as a diet marker, this test was approved in the past mentioned process [29]. Before the test, the rats were separated keen on five groups of 6 rats each, and they were given an 18-hour fast. Castor oil was given to each group to induce diarrhea. All rats were administrated 1 ml of 10% charcoal suspension in 5% gum acacia as a continuous media, orally after 1 hour of medication delivery. All of the rats were slaughtered an hour later, and the amount of intestinal distance that the charcoal meal, caecum was calculated and reported as a % of total distance traveled [30].

2.11. Data analysis

Every analysis was performed three times. The data was shown as mean ± SEM. The significance of the

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dissimilarity between the control and test groups was ascertained with one-way analysis of variance (ANOVA), after which the Student's t-test was utilized a significant P value of 0.05 or 0.01 was indicated.

3. Results

3.1. Extraction value

After the maceration process, 65 g of root powder weighing 13% of the total was recovered.

3.2. Phytochemical screening

Moringa oleifera crude root extract contained alkaloids, saponins, flavonoids, tannins, phenols, terpenoids, and steroids, according to a preliminary phytochemical screening test. However, neither glycoside nor anthraquinones were present (***Table 1***).

Table 1: Analysis for the presence of different phytochemical compound in HAE-AT leaves.

Constituent	**HAE-AT leaves**
Alkaloids	+
Saponins	+
Flavonoids	+
Tannins	+
Phenols	+
Terpenoids	+
Glycoside	-
Anthraquinones	-
Steroids and Sterols	+

+ = Present; - = Absent

3.3. Acute oral toxicity test

For the first 24 hours and the next 14 days, the ethanolic extract root extract of *Moringa oleifera* did not result in any mortality at a particular limit test dose of 2000 mg/kg, according to the study. Furthermore, no significant overt toxicity indicators or symptoms, like behavioral, mental, or physical abnormalities, were observed in the toxicity investigation.

3.4. Effects of the ethanolic extract on castor oil-induced diarrheal model

The ethanol extracts significantly decreased the amount of diarrhea that the rats had in the castor oil-induced test. When compared to untreated control rats, ethanol extract significantly reduced the frequency of defecation ($P<0.05$). When compared to the rats who received castor oil treatment, the extract reduced the overall quantity of wet feces that were generated after being administered (**Table 2:** presents the findings).

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Table 2: Effect of ethanolic extract of *Moringa oleifera* root on castor oil induced diarrhea in rats.

Treatment/ Dose (mg/kg)	**Mean defecation in 4 Hr.**	**% inhibition of defecation**
Castor oil + Control (saline 2 ml/kg i.p)	21.32 ± 2.7039	----------
Castor oil + Atropine(3mg/kg i.p)	14.20± 0.9098	33.37 **
M. oleifer (100mg/kg i.p) + Castor oil	11.14 ± 0.8027	47.65**
M. oleifer (200mg/kg i.p) + Castor oil	9.31 ± 1.8236	56.23 ***
M. oleifer (400mg/kg i.p) + Castor oil	8.17 ± 1.3017	61.75 ***

Values are expressed as mean ± SEM from the experiments. *P<0.05, **P<0.01, ***P<0.001 when compared with CO+ saline treated group.

3.5. Effects of the ethanolic extract on castor oil-induced enteropooling

In the castor oil-induced entropooling test, the *Moringa oleifera* crude root extracts have an apparent effect (Table *3*). When the extract was used, the intestinal volume was reduced by 28.67% and 25.45%, respectively. The extract's action was less strong than that of the standard drug, which also considerably decreased intestinal fluid buildup (P<0.01).

Table 3: Effect of ethanolic extract of *Moringa oleifera* root on castor oil induced enteropooling in rats.

Treatment/ Dose (mg/kg)	**Mean defecation in 4 Hr.**	**% inhibition of defecation**
Castor oil + Control (saline 2 ml/kg i.p)	7.11 ± 0.1227	----------
Castor oil +Atropine (3 mg/kg i.p)	5.35± 0.2054	24.53 *
M. oleifer (100mg/kg i.p) + Castor oil	3.21 ± 0.1163	54.41**
M. oleifer (200mg/kg i.p) + Castor oil	1.95 ± 0.0497	72.07 **
M. oleifer (400mg/kg i.p) + Castor oil	1.24 ± 0.1172	82.52***

Values are expressed as mean ± SEM from the experiments *P<0.05, **P<0.01, ***P<0.001 when compared with CO+ saline treated group.

3.6. Gastrointestinal motility test

The ethanolic extract considerably (P<0.01) reduced the gastrointestinal distance that the rat's charcoal meal diet covered compared to the control group. The result shown in Table 4 is that the propulsion of charcoal meal through the intestinal tract was significantly reduced (41.06%) by Loperamide (5 mg/kg).

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Table 4: Effect of ethanolic extract of *Moringa oleifera* root on castor oil induced small intestinal transit in rats.

Treatment/ Dose (mg/kg)	Total length of intestine	Distance traveled by marker	% inhibition of defecation
Castor oil (1ml p.o) +Control (saline 2 ml/kg i.p)	113.65 ± 2.86	97.5 ± 3.02	84.66 ± 1.05
Castor oil + Atropine (3 mg/kg i.p)	106.21± 2.82	42.65 ± 2.76	40.57 ± 1.14**
M. oleifer (100mg/kg i.p) + Castor oil	98.54 ± 4.82	51.50 ± 4.35	51.76 ± 2.62*
M. oleifer (200mg/kg i.p) + Castor oil	107.33 ± 3.04	45.23 ± 1.74	41.59 ± 0.96 **
M. oleifer (400mg/kg i.p) + Castor oil	102.68 ± 3.04	39.58 ± 2.761	37.28 ± 2.62***

Values are expressed as mean ± SEM from the experiments *P<0.05,*P<0.01, **P<0.001 when compared with CO+ saline treated group.

4. Discussion

On the go metabolite of castor oil is released in lipase in the upper section of the small intestine and causes diarrhea [31]. This acid produces inflammation and prostaglandin release by irritating the intestinal mucosa [32]. Additionally, the prostaglandins that are secreted encourage the small intestine to secrete water and electrolytes. Prostaglandins also increase intestinal mucosal edema, gastrointestinal motility, and epithelial permeability, which inhibits the reabsorption of water and sodium chloride [33,34]. Additionally, research has shown that castor oil's diarrheagenic effects are related to its production of cytotoxic impact in intestinal absorptive cells by inhibition of sodium-potassium ATPase [35,36]. Our use of castor oil as a GI motility and secretion inducer in this investigation is supported by this mechanistic evidence.

Since castor oil is a good standard for examining the anti-diarrheal consequence and generates diarrhea in a manner comparable to the normal pathophysiological processes, diarrhea was artificially caused in the present investigation [37]. It is commonly known that lipases react with castor oil to produce ricinoleic acid, the active ingredient. As a result of ricinoleic acid's annoyance and swelling of the gastrointestinal mucosa, prostaglandins are produced. These changes in mucosal permeability, intestinal peristalsis, and electrolyte movement cause diarrhea and hypersecretion [38]. According to studies, activated charcoal efficiently adsorbs chemicals, including medications, on the intestine's surface to prevent absorption [39].

Thus, to investigate the impact of *Moringa oleifera* on peristaltic movement, charcoal meal research was utilized. In this model, the ethanolic root extract of *Moringa oleifera* demonstrated a significant difference (P <.05) across all test doses. The extract had a dose-dependent impact on this animal, suggesting that the maximum dose (400 mg/kg) has the most anti-diarrheal efficacy, with a 50.7% reduction in defecation. This was consistent with recent results that reported a peak anti-diarrheal action of a high dose of *Moringa oleifera* ethanolic root extract [40,41]. The anti-diarrheal effect of *Moringa oleifera* root has been experimentally verified to possess anti-oxidant activity in vitro [42]. Non-steroidal anti-inflammatory medications have been shown in scientific literature to postpone the onset of diarrhea caused by castor oil. Similar results have been demonstrated by Moringa oleifera root extract, which may be related to its anti-inflammatory qualities [42].

Using intestinal enteropooling and anti-motility models, the likely mechanism of action of the root extract of *Moringa oleifera* was investigated in order to validate its anti-diarrheal effect. This result suggested that the root extract had an anti-secretory impact, suggesting that this could be one of the mechanisms behind its anti-diarrheal properties. This discovery suggests that the

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plant might be a viable choice for creating innovative medications with anti-diarrheal properties.

5. Conclusion

The outcome of the research suggested that the extract of roots of *Moringa oleifera* may possess anti-diarrheal properties; this could be since it inhibits both fluid output and intestinal motility. The plant's anti-diarrheal properties may be attributed to the secondary metabolites found inside it, which could work through multiple methods. To identify and isolate the ingredient that acts in the extract as well as to determine its exact mechanism of action, more investigation is required.

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Ethical approval

The experimental protocols using laboratory animals were requested to and approved by the Institutional Review Board (*Ref. No. IAEC/2019/22)*, IFTM University, Moradabad, U.P. India.

Conflict of Interest

The authors do not have any conflict of interest.

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