EVALUATION OF ANTI-DIARRHEAL ACTIVITY OF STEM BARK OF *OROXYLUM INDICUM* ON EXPERIMENTAL ANIMALS

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ABSTRACT

The goal of this study was to evaluate the anti-diarrheal properties of the ethanolic extract of stem bark of *Oroxylum indicum* in castor oil induced rats. Animals were randomly divided into four groups, each group consisting of 6 animals: (Group-1) Normal Control group, (Group-2) Positive control group treated with standard drug (Loperamide, 5 mg/kg, orally), (Group-3) Treatment group (Low dose) treated with *Oroxylum indicum* stem bark extract (200mg/kg, orally) and (Group-4) Treatment group (High dose) treated with *Oroxylum indicum* stem bark extract (400mg/kg, orally). The animals of treatment group showed significant deterioration in gastrointestinal floras which cause a significant increase in the movement of the charcoal meal, weight of intestinal content, volume of intestinal content, and percentage inhibition. Treatment with ethanolic extract produced dose dependently significant improvement in gastrointestinal function by preventing the wet sewage production, restricting the passage of enteropooling caused by castor oil, which lowers the weight and volume of intestinal content, decreases mean number of Wet/loose faeces in 5hrs, also significantly increase the movement of the charcoal meal. These findings suggest that the ethanolic extract of the stem bark of *Oroxylum indicum* possesses anti-diarrheal properties in dose dependent manner. As a result, this plant may have some medicinal potential in humans for the treatment of diarrhea.

KEYWORDS: Castor oil, *Oroxylum Indicum* and Diarrhea.

1. INTRODUCTION

In clinical practise, patients with diarrhoea are frequently treated for the disease. Due to individual differences in habits, a precise description of diarrhoea is difficult to come by, but it is typically understood to mean frequent defecation more than three times per day, loose and unhygienic faeces, or an abnormal rise in the total amount and water content of stools **[1]**.

Diarrhea can include gastrointestinal problems such as fever, abdominal pain, or vomiting. It is related to imbalances in controlling absorption and diarrhea associated with hypermotility leading to excessive loss of body fluids and electrolytes in the faeces and its causes are different. Currently, it is a rapid and effective primary cause of malnutrition and infant mortality in poor nations! **[2]**.

Diarrhea is a disorder of the gastrointestinal system regarded as bloating, frequent, high levels of faecal fluid matter that is known as watery stools. The main reason for diarrhea is greater bowel movements, short absorption time, and a large volume of fluid in the delivery of the large intestine as well as full dimensions to absorb salts, electrolytes, and water. It can be produced by any type of allergy, toxic substances, unhealthy foods, or poor hygiene **[3]**.

Diarrhea is the most important cause of illness and mortality throughout worldwide. Poor hygiene, mess, and bed food are the cause of approximately 88% of diarrheal-related deaths. Diarrhea is a serious global health problem which responsible for more than 5 to 8 million deaths in children under the age of 5 every year, especially in developing countries **[4].**

Diarrhea is the continuous passing of loose, aqueous, and discoloured faeces. Water loss through diarrhea may lead to dehydration and imbalance of electrolytes and maybe die in the last **[5].**

The maximum common cause of diarrhea is intestinal infection by a virus, bacteria, or maybe parasite, and this situation is known as ‘gastroenteritis’. This infection mostly occurs from food or water contaminated by faeces or directly caused by another pre-infected person.

At the current time, some advanced pharmaceuticals offer various drugs for diarrhea but show large health-related problems in people in countries of tropical and subtropical regions.

This is one of the main reasons of foremost reasons for death, especially in children of 5 years of age **[6].**

The imbalance between the secretary mechanisms and absorption intact of the intestine results in an excessive loss of water in faeces which causes diarrhea. Inhibition of diarrhea experimentally depends on the potency of anti-diarrheal agents pharmacologically.

Certain anti-diarrheal substance exhibits their effect through the decrease of gastrointestinal motility and also excretion.

Diarrhea is one most common reason to seek medical advice for people. It can range from mild to temporary conditions and then can be life-threatening conditions. About two billion cases are found every year of diarrhea and about 1.9 million cases are found in children under the age of five years globally and mostly found in developing countries in which most cases results in death from diarrhea **[7].**

1.2 SYMPTOMS OF DIARRHEA

The most typical cause of diarrhoea is dehydration. In dehydration, electrolytes are lost which is the water amount present in the body, and muscle activity and other required functions are affected. It's individually dangerous for children, old age adults, and people which have poor immune system. Dehydration is mostly treated to avoid severe health problems, like damage to organs, shock, unconsciousness, and other serious problems **[8].** In children, acute diarrhea is treated with an oral rehydration solution.

1.3 TREATMENT OF DIARRHEA

Drugs used for symptomatic diarrhea in adults

Codeine

Codeine is a type of pregnancy category C & schedule H drug. The indication of codeine drug is short-term symptomatic relief in adults. It also relieves pain. This drug is available in tablet form, at a dose of 30mg. The dose is given to an adult 3 to 4 times per day for relief from acute diarrhea.

In the condition of peristalsis inhibition, the drug is avoided, when distension of the abdominal then this drug is not used. In the cases of acute diarrheal like ulcerative colitis or colitis associated with antibiotics and in acute depression respiratory the drug must be avoided.

This drug creates tolerance and dependence when prolonged use. It occurs with hepatic and renal impairment so this drug is used with precaution **[9].**

Loperamide

Loperamide is used for the control and treatment of diarrhea and relief of acute unspecific acute and chronic diarrhea caused by inflammatory diseases or gastric infections.

It is available in form of tablets or capsules of 2 mg; and in liquid form in 1 mg/5 ml. It is used orally. The dose fixed for an adult is 4 mg and then 2 mg after every motion, and for a child 2mg followed by 2mg after every motion.

In the conditions where peristaltic inhibition, drugs should be avoided, where distension abdominal develops, or in those conditions in which active ulcerative colitis or antibiotic-associated colitis. In case of the disease in the liver; pregnancy occurrence, glaucoma; or Crohn's disease, obstruction in the urinary bladder is used within precautions.

Loperamide drugs have adverse effects are cramp the abdomen, dizziness, drowsing, and skin related like urticaria, dry mouth, retention of the urinary tract, etc. It is degraded when comes in contact with light and moisture so it is stored and protected from light and moisture. **(NFI4thEdition, 2011) [10].**

2. MATERIALS AND METHODS

2.1 Plant material and chemicals

Oroxylum indicum is a very common herbal plant. Parts of the plant are used in various diseases and disorders of the human body. The stem bark was collected from a botanical garden in Meerut, Uttar Pradesh (India). The stem bark was packed and maintained in a herbarium file and transferred to the Botanical Department of the **Chaudhary Charan Singh University**, **Meerut** for authentication with **reference no. Bot/PB/152**. The taxonomical identification of the plant was done by **Prof. (Dr.) Vijay Malik, Department of Botany, Chaudhary Charan Singh University, Meerut.** All chemicals and reagents used were of analytical grades, castor oil **(**laxative), saline (0.9% NaCl), charcoal powder (10% activated charcoal in 0.5% w/v sodium carboxymethyl cellulose), and vehicle (0.5% w/v sodium carboxymethyl).

2.2 Extraction procedure

The *Oroxylum indicum stem bark* was collected and dried in shade and then dried bark was powdered mechanically by grinder and mixer and pass-through sieve (no. 40). After this about 300gm of bark, and dust was packed in soxhlet apparatus and extraction was carried out by ethanol. Liquid extract was evaporated till the brownish-semi solid mass was obtained.

2.3 Phytochemical analysis

The phytochemical evaluations were conducted for the identification of constituents. Phytochemical evaluation tests were done to find out the presence of pharmacologically active chemical components like alkaloids, flavonoids, glycosides, terpenoids, steroids, tannins and also phenols, and other constituents like reducing sugars, proteins and carbohydrates and also amino acids, etc. by using standard procedures.

2.4 Experimental Animals

The experiment was done for the investigation of the effect of ethanolic extract of stem bark of *Oroxylum indicum* on castor oil-induced diarrhea. The investigational procedures were permitted through the Institutional Animal Ethics Committee (IAEC) by reference no. **IAEC/MIET/2022/83/Dt17/09/2022**. 42 Wistar rats weighing 200g-250g of either sex were carefully chosen. Rats were starved for 12 hours before the experiment but were allowed free access to water and were housed in polypropylene cages under ordinary

circumstances of the light cycle of 12 hrs light/dark cycles and temp of 25ºC ± 5ºC, for seven days before the experimentations. Rats were allowed to acclimatize for research laboratory conditions before experimentation.

2.5 Pharmacological Screening

2.5.1 Antidiarrheal test:

The animals for the test were starved for 12 hours before experiments but were allowed free access to water. The antidiarrheal test was performed as per the standard procedures using the experimental design given above. The rats were then housed singly in cages lined with white blotting paper. The rats were administered 2 ml of castor oil orally after 01 hour of the above treatments. The rats were observed at time intervals, up to 5 h after the castor oil administration, for the presence of diarrhea. Diarrhea was taken to mean watery (wet), unformed stools. The number of wet droppings was counted every hour for a period of 5 hrs **[11]**.

2.5.2 Castor oil induced enteropooling:

After 30 min of the administration of ethanolic extract of stem bark of *Oroxylum indicum*, 2ml of castor oil was orally given to every animal. After 30 min. of castor oil, the animals were sacrificed by overdose of anaesthetic agent and whole part of intestine from pylorus to ceacum was dissected and contents of it were collected in the examination tube and volume was measured **[12]**.

2.5.3 Charcoal meal test:

The animals for the test were starved for 12 hours before experiments but were allowed free access to water. The charcoal meal test was performed as per the standard procedures using the experimental design given above. Later 30 minutes, the diarrhea was produced by oral administration of 2ml of castor oil to each rat. Every rat was kept in the house in separate cages, the floor of the cage was lined with the blotting paper. Every hour changed the lining of the floor. Animals were continuously observed for four hrs, and charcoal meal content was noted in the rats **[13]**.

2.6 Statistical analysis

The mean±SEM was used to express all values. One-way ANOVA was used for the statistical analysis, and Tuckey's test was used for the post hoc analysis. $p<0.05$ was considered significant.

3. RESULT

3.1 Acute Toxicity Studies

According to OECD guidelines 423, the acute toxicity of ethanolic extract was assessed. The animals were put into four groups of three rats each, with doses of 5, 50, 300, and 2000 mg/kg. The animals were observed for 3 hours for any sign and symptoms. Then animals were observed for 14 days for behavioural abnormality, dermal toxicity, salivation and lacrimation and any mortality. Wistar rats showed no mortality and no sign of toxicity at any dose level. So ED50 was calculated by $1/10^{th}$ of 2000mg/kg that is 200mg. Since 200mg/kg was safe dose, two doses were selected that is lower dose (200 mg/kg) and high dose (400 mg/kg).

3.2 Phytochemical analysis

The extract gave positive tests for different phytoconstituents viz. tannins, alkaloids, and flavonoids (Table 1).

3.3 Effect of *Oroxylum indicum* stem bark ethanolic extract on castor oil induced diarrhea

On treatment with 200 mg/kg and 400 mg/kg of ethanolic extract of *Oroxylum indicum* showed a substantial decrease in mean number of loose faeces from 10.5 to 6.0 respectively and percent inhibition from 44.73% to 68.43% respectively as compared to the mean number of faeces 19.0 in control group with 0% inhibition. Whereas standard loperamide decreases the number of loose faeces upto 4.8 and causes the 74.5% of inhibition. The *Oroxylum indicum* stem bark ethanolic extract on the doses of 200 mg/kg & 400 mg/kg decrease the occurrence of excretion and the whole mass of faeces significantly (Table 2).

3.4 Effect of *Oroxylum indicum* stem bark ethanolic extract on castor oil enteropooling in rat

Castor oil caused accumulation of water and electrolytes in intestinal loop. Treatment with the *Oroxylum indicum* stem bark ethanolic extract (200 and 400 mg/kg) produced a significant and dose-dependent reduction in intestinal weight and volume 45.13 to 59.72% and 36.95 to 50.0 % respectively as compared to control group with no inhibition in weight and volume of intestinal content. Where as standard drug loperamide reduces the weight and volume of intestinal content by 67.02 and 58.69% respectively. The ethanolic extract of stem bark of *Oroxylum Indicum* showed a dose-dependent anti-diarrheal effect by significantly improving the weight and volume of intestinal content (Table 3).

3.5 Effect on charcoal meal

The mean expanse moved with charcoal meal markedly decreased with 200 mg/kg and 400 mg/kg of ethanolic extract of *Oroxylum indicum* by 60% and 33.8 % as compared to the control group i.e. 79%.

Moreover, Percent of inhibition (%) on treatment with 200 mg/kg and 400 mg/kg of ethanolic extract of *Oroxylum indicum* significantly decrease by 24.05% and 57.17% as compared to the normal control group. On comparing both 200 mg/kg and 400mg/kg doses treatment groups, a less significant extent of small-intestine, movement of charcoal meal and percent of inhibition (%) was observed. This revealed that stem bark ethanolic extract at a dose of 200mg /kg slowed the flow of charcoal feed in rats associated with the control group. But an amount of 400 mg/kg of extracts from the bark of the stem does not express any substantial effect; it shows a delay in the flow of charcoal powder in animal experiments.

Based on the above observations, we can conclude that treatment with a low dose did not show a substantial effect but at a high dose showed their effect close to the normal effect and the results were statistically significant (Table 4).

4. DISCUSSION

Diarrhoea has long been considered one of the most common well-being issues in growing nations. Imbalance in the absorption and excretion of fluid causes regular harm to fluid (diarrhea). Several methods are recommended to explain the outcome of castor-oil induced diarrhea which includes inhibiting the intestinal function of Na+K+ATPase, thereby reducing

the intestinal fluid accumulation, instigation of adenylate cyclase or mucosal cAMP arbitrated excretion, and promoting prostaglandin release **[14].**

Oroxylum indicum is a herbal plant having therapeutic value in various diseases like hepato toxicity, hyperglycemia, and infectious diseases. It has also been shown to be very effective in wound curing due to its phytoconstituents.

The phytochemical study showed that the stem bark of *Oroxylum indicum* includes alkaloids, flavonoids, saponins, steroids, terpenoids, and other minerals. These phytoconstituents might negate the traditional usage of that plant's stem bark to regulate the level of microbial and fungal toxins. The primary phytochemical constituent tannins changes to tannates' constituent proteins to prevent the invasion of the abdominal mucosa, which lessens gastrointestinal tract sensitivity and irritation **[15].**

This study included the investigation of antidiarrheal activity of ethanolic stem bark of *Oroxylum indicium* in castor oil induced diarrhea in rats with loperamide as standard. The use of the diarrhea model caused by castor oil is due to the release of autocoids and prostaglandins. Ricinoleic acid from castor oil causes irritability and swelling of the duodenal mucosa primarily to the release of prostaglandin that stimulates motility and excretion. Rats treated with castor oil presented a substantial growth in water content mass, and faecal substance intake associated with a normal rat. The ethanolic stem bark extract of *Oroxylum indicum* has shown a significant drop in water, and dietary faecal matter compared to control rats. This indicates that the extracted plant has an anti-diarrhoeal effect.

Magnesium sulfate is an osmotic laxative. It causes diarrhea by endorsing the discharge of cholecystokinin from the intestinal mucosa which prevents the re-absorption of sodium chloride and aquatic into the lumen. Loperamide has antidiarrhoeal action for both castor oil and magnesium-induced diarrhea. The widely used medication loperamide has one of the most significant impacts. Loperamide is an agonist of the mu-opioid receptor that promotes colonic and local motility. Limitations are water content and food eating and mass of fecal substance within four hrs **[16].**

Loperamide decreases diarrhea caused by castor-oil, and prostaglandin efficiently. It too decelerates duodenal movement, colon flow rate, and colon motility. Decreased bowel

movement is associated with impaired calcium ion penetration by digested calcium channels **[17].**

Loperamide is an artificial medication that is broadly used in the cure and control of diarrhea, and though comparatively safe in terms of dosage, life-threatening loperamide can cause a novel clinical trial of loperamide poisoning. Other symptoms might be faintness, abdominal ache, uneasiness or swelling, nausea, dry mouth, and faintness. The plant extract of *Oroxylum indicum* are similarly used in the cure of diarrhea as they may have fewer side effects than loperamide.

On the basis of the literature survey of traditional medicinal plants, *Oroxylum indicum* shows various pharmacological activities as antipyretic, anti nematodal, diuretic, anti helminthic, anti-yeast, antiulcer, anti fertility, anti malarial, antifungal, antiviral, anti hyperglycemic, anti spermatogenic, anti-inflammatory, hyper cholesteremic, antispasmodic, immune modulator, insecticidal, antitumor, hypoglycaemic, etc. The present research work is hypothesized based on a literature survey.

Other parts such as the leaves and roots of *Oroxylum indicum* show the anti diarrhoeal effects due to the presence of chemical constituents tannins, alkaloids, and other chemical constituents which are responsible for the anti diarrhoeal activity. The study is conducted on the base of chemical constituent ‘Tanins' which are responsible for the anti diarrhoeal activity.

The phytochemical study of the *Oroxylum indicum* bark founds evidence for the presence of chemical constituents like tannins, alkaloids, and other chemical constituents which may be responsible for the anti diarrhoeal activity.

Treatment with ethanolic extract of stem bark of *Oroxylum indicum* at 200mg/kg and 400mg/kg causes substantial improvement in weight and volume of intestinal content and mean number of wet/loose faeces as compared with control rats. Ethanolic extract presented substantial anti-diarrhoeal action but is lower than standard loperamide treated rats. *Oroxylum indicum* at a dose of 200mg/kg and 400mg/ kg displayed substantial reduction in mass of colonic content. This indicates that *Oroxylum Indicum* is effective in the cure and control of diarrhea.

The charcoal meal hyperperistalsis model is used to examine *Oroxylum indicum* anti diarrhoeal action using the length of the small intestine, the distance travelled through charcoal diet limits to calculate the percentage inhibition. Reducing bowel movements is one of the ways anti diarrhoeal agents can show their action. It was noted that *Oroxylum indicum* severely restricted the processing of charcoal meal at all tested levels. These findings suggest that these extracts have the potential to influence peristaltic bowel movements thus representing the occurrence of anti-motility action.

So we can say *Oroxylum indicum* bark has anti-diarrhoeal properties. The stem bark of *Oroxylum indicum* has bulkiness properties that are also responsible for anti diarrhoeal potential.

5. Conclusion

The ethanolic extract of *Oroxylum indicum* significantly decreased intestinal motility and prevented the rat ileum's contractions brought on by castor oil. The anti diarrheal action that has been noticed may be a result of these effects.

Treatment with ethanolic extract of stem bark of *Oroxylum indicum* at 200mg/kg and 400mg/kg causes substantial improvement in weight and volume of intestinal content and mean number of wet/loose faeces as compared with control rats.

It was noted that *Oroxylum indicum* severely restricted the processing of charcoal meal at all tested levels. These findings suggest that these extracts have the potential to influence peristaltic bowel movements thus representing the occurrence of anti-motility action. This indicates that *Oroxylum Indicum* is effective in the cure and control of diarrhea.

More research is required to pinpoint the precise mechanism of action of ethanolic extract on ileal smooth muscles.

Table 1. Chemical constituents of *Oroxylum Indicum* stem bark ethanolic extract

S.No.	Phytochemical Constituents	Name Of Tests	Results
1.	Alkaloids	Mayer's test	Present
		Hager's test	Present
		Dragendorff's test	Present
2.	Carbohydrate and reducing sugar	Molisch's test	Present
		Benedict's test	Present
3.	Tannins	Ferric chloride test	Present
4.	Saponins	Froth test	Absent
5.	Glycosides	Modified Borntrager's Test	Present
		Legal test	Present
6.	Flavonoids	Alkaline reagent test	Present
7.	Protein and amino acid	Ninhydrin test	Present
8.	Terpenoids and steroids	Salkowski's test	Present

Table 2: Effect of *Oroxylum Indicum* stembark ethanolic extract on castor oil induced diarrhea.

Groups	Dose	Mean number of Wet/loose faeces in 5hrs	Percent inhibition (%)
Normal Control group	1ml/100gm	19±1.269	0
Castor oil + Loperamide	2ml+5mg/kg	4.8±0.705^{a***}	74.50%
Castor oil + Extract	2ml+200mg/kg	10.5±0.849^{a***}	44.73%
Castor oil + Extract	2ml+400mg/kg	6±0.634 ^{a***}	68.43%

Values are expressed as mean±SEM (n=6).

Significantly different from control group ^{a***} $p < 0.001$.

Table 3: Effect of *Oroxylum Indicum* stembark ethanolic extract on castor oil-induced enteropooling

Groups	Dose	Weight of intestinal content (g)	Percent inhibition (weight) (%)	Volume of intestinal content (mL)	Percent inhibition (volume) (%)
Control group	1ml/100g	3.08±1.20	0	1.91±0.375	0
Castor oil + Loperamide	2ml+5mg/kg	1.01±0.506^{a**}	67.02%	0.79±0.119$^{a\#}$	58.69%
Castor oil + Extract	2ml+200mg/kg	1.69±0.830^{a*}	45.13%	1.20±0.228	36.95%
Castor oil + Extract	2ml+400mg/kg	1.24±0.600$^{a\#}$	59.72%	0.95±0.136^{a*}	50%

Values are represented as Mean±SEM, of n=6 per group. Where ^{a**}p<0.01, ^{a*}p<0.05, $^{a\#}$p<0.02 when compared to control group.

Table 4: Effect of *Oroxylum Indicum* stembark ethanolic extract on charcoal meal test

Groups	Dose	Movement of charcoal meal (%)	Percent of inhibition (%)
Normal Control group	1ml/100g	79±1.719	0
Castor oil + Loperamide	2ml+5mg/kg	27.6±1.526^{a***}	64.98%
Castor oil + Extract	2ml+200mg/kg	60±1.533^{a***}	24.05%
Castor oil + Extract	2ml+400mg/kg	33.8±1.606^{a***}	57.17%

Values are represented as Mean±SEM, of n=6 per group. Where ^{a***}p<0.001when compared to control group.

Figure -1

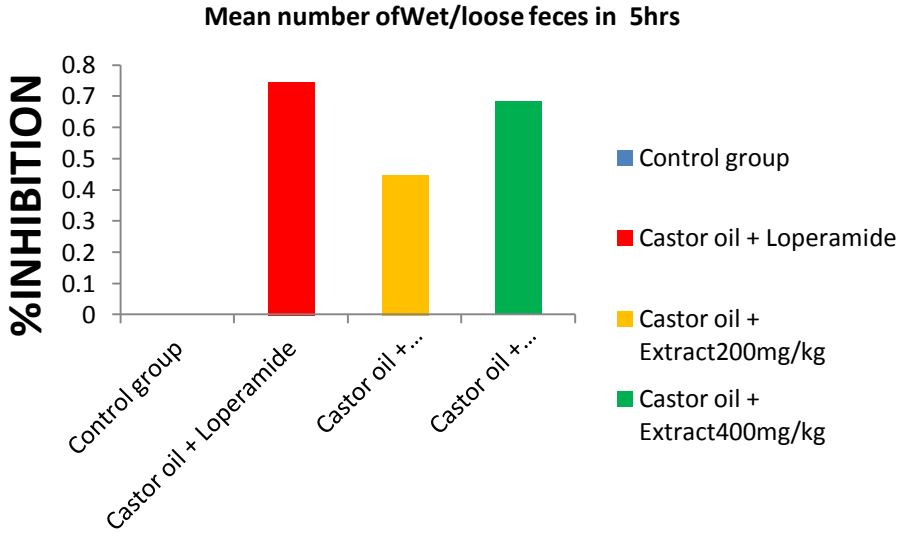


Figure -2

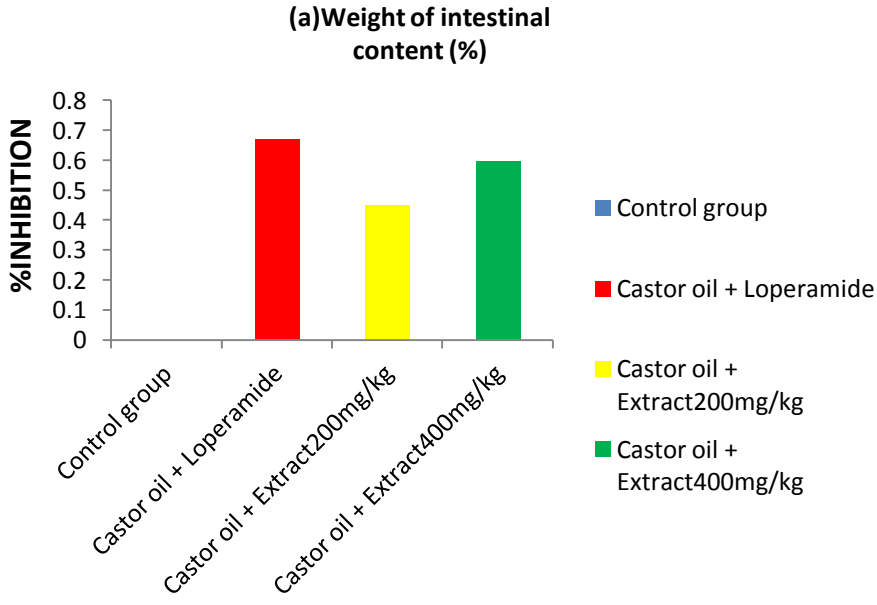


Figure -3

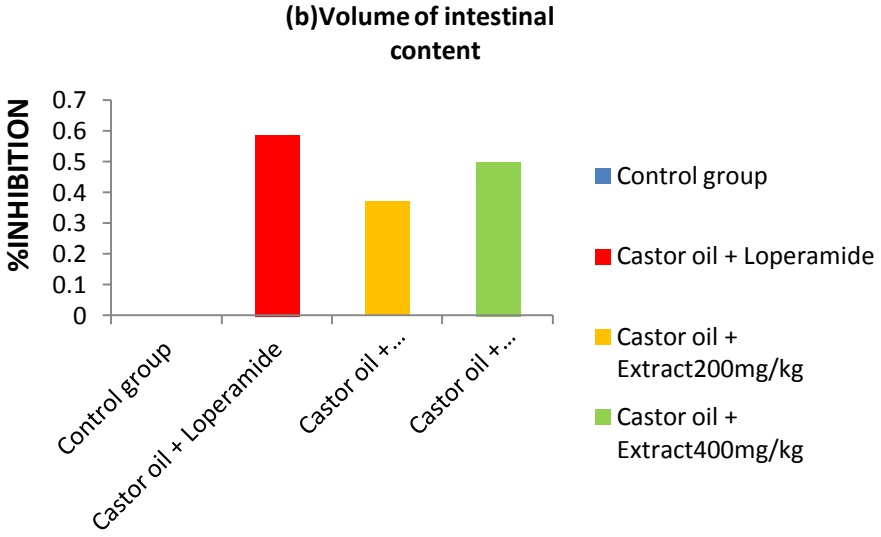
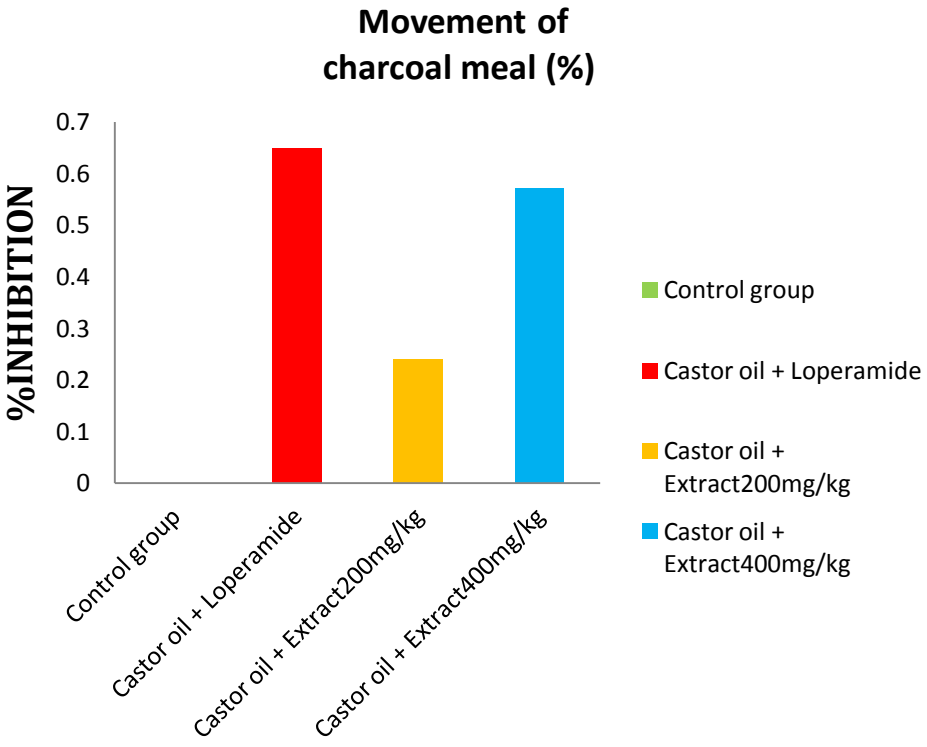


Figure -4



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