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## Research



### A Screen Myrtuscommunis And Lantana Camara Extracts For Their Anti Diarrheal And Anti-Spasmodic Activity By Swiss Albino Mice Models

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	<b>Abstract</b>
Published on: 01 Feb 2024	<p>Presently, around 25% of medications produced in the globe, are extracted straight from plants or herbs contains at least one active component. It is acknowledged that the popular of herbal medicines employed as antidiarrheals have antispasmodic characteristics consequential in delaying gastrointestinal procedures, inhibiting gut motility, initiating absorption of water and dropping electrolyte discharge in the process, and these biological activities might explain the benefits of by means of specific herbal medicines in the management and treatment of diarrhoea. The main aim of the study is to screen Myrtuscommunis and Lantana camara extracts for their anti-diarrheal and anti-spasmodic activity. This study was intended to assess the antidiarrheal activity of the selected herbs by means of Swiss albino mice models against castor oil stimulated diarrhea, castor oil stimulated gastrointestinal transit, and castor oil stimulated accumulation of gastrointestinal fluid. In the execution of antimotility, diarrhea, and anti-secretory agent are seem to be the chief stay agents utilized to drop off the pathophysiologic circumstances accountable for the progress of diarrhea. The inhibitory force of loperamide on acetylcholine cause inhibition of discharge intervened with acetylcholine. As an outcome, loperamide lessen every day fecal volume, reduce fluid and loss of electrolyte, and may perhaps augment viscosity of stool and bulk density. Coming to the Myrtuscommunis and Lantana camara, the result of the study verified that the plant extracts was caused a noteworthy impediment in the onset of diarrhea, reduction in the occurrence of output of wet fecal and total fecal, along with diminish in the mean weight of wet feces and output of total fecal that were caused by means of castor oil. The plants extracts established a noteworthy delay in the onset of diarrhea, abridged the occurrence of wet feces and also endowed with noteworthy anti-secretory effects at all doses assessed experimentally. And also, the plants extracts signified the antimotility activity at its higher doses.</p>
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## INTRODUCTION

Diarrhoea is a principal killer of children, accounting for roughly 8% of all deaths amid children below age 5 worldwide in 2017. This explains to over 1,300 young children dying every day, or around 480,000 children a year, in spite of the accessibility of simple effective treatment. Most deaths from diarrhoea happen amongst children below 2 years of age living in sub-Saharan Africa and South Asia. In spite of this heavy toll, progress is being made. From 2000 to 2017, the over-all annual number of deaths from diarrhoea amid children below 5 lessened around 60 per cent<sup>6</sup>. Diarrhoeal ailments are usual amongst inpatients and outpatients particularly in developing parts of the globe. Acute diarrhoea is well-defined as the passage of 3 or more loose or liquid stools per day<sup>2</sup>. Few definitions necessitate the passage of raised frequency of stools of reduced form from the usual long-lasting for 14 days. Persistent diarrhoea persists amid 14 days to 30 days although chronic diarrhoea continues beyond a month. Acute diarrhoea of infectious aetiology is discussed to as gastroenteritis too. Few of these infections might present mostly with vomiting and nausea<sup>3</sup>. Additional symptoms comprise cramps, abdominal pains, fever, flatulence, bloating, tenesmus and blood in stools. Diarrhoeal ailments might outcome in malnutrition and chronic complications in children below 5 years. Diarrhoea is caused by means of infections, frequently spread from individual to individual or contaminated sources, water contaminated with animal feces or human and other causes as well as poor personal hygiene, food maintenance in unhygienic conditions and malnutrition. Cases of dysentery frequently do not have identifiable agent<sup>5</sup>. Maximum cases of acute diarrhoea are self-limiting and need not require treatment. For the additional chronic cases, the mainstay of treatment is supportive in the procedure of rehydration and infrequently definite antimicrobial treatment<sup>6</sup>. Castor oil induced diarrhea is one of the widely used model for evaluation of effectiveness of novel drugs and medicinal plants<sup>9,10</sup>. *Myrtis communis* shown antimicrobial, antifungal, insecticidal, anti-inflammatory etc and *Lanata Camara* proved effective in antimicrobial, anti-fungal, anti-viral, anti-oxidant, wound healing activities etc.

## MATERIALS AND METHODS

### Plant Collection and Extraction

i) Fresh plants material parts were collected and authenticated through registered botanist Dr Madhavachetty, SVU, Tirupati. Then the plants material was extracted using methanol solvent by means of utilizing soxhlet extractor awaiting the color in siphon tube become colorless. Collected liquid extract was filtered out and extract concentrated by means of utilizing rota evaporator. Resulting extract was packed in a container and amassed in refrigerator.

ii) Later than extraction phytochemical screening and bio active constituents characterization study was finished by means of employing suitable methods<sup>95</sup>.

### Experimental animals

Six weeks old Male wistar rats were procured from Nirmala college of Pharmacy. All experimentation and procedures carried out on the animals (rats) were approved by the Institutional Ethics Committee of Nirmala College of Pharmacy. Rats were housed in a proscribed temperature of room at 25±1 °C under standard mentioned surroundings (12-h dark-light cycle). They were housed in a polypropylene cage and presented food and water ad libitum. Animals were quarantined and become familiarized laboratory conditions for 7 days before scheduled to study initiation. Animals were observed for common health and suitability for investigation during this phase.

### Acute Toxicity

Before beginning of animal investigation, the acute toxicity study (according to OECD guideline) was carried out to established effective dose of test compounds. Based on findings of acute toxicity, the lead extracts were tested in suitable diarrhea model<sup>96</sup>.

### In-Vivo Study<sup>97-100</sup>: Experimental Animals

Swiss albino mice weighing 20 to 30 g of age 6 to 8 weeks were employed for the experimentation. The mice were housed in plastic cages at 22±3 Centigrade and on a 12-hour light and 12hr dark cycle amid accessible to food pellet and water ad libitum. Good hygienic conditions were maintained by means of constant cleaning and exclusion of feces as of cages 3 times a week. The mice were habituated to laboratory surroundings for 1 week proceeding to the experimentation. Food was taken out 18 hrs proceeding to the commencement of all the experiments. The care and treatment were based on international guidelines for the utilization and upholding of experimental animals.

### Grouping and Dosing of Animals

Mice were randomly assigned into 6 groups of 2 plant test extracts (2 dose groups for each extract) treated, 1 disease control group and standard group with 5 mice per each group.

**Table 1: Grouping of Animals**

Group name	Treatment	Dose / Route
Control	Normal Diet	
Disease control	<i>Distilled water + Castor oil</i>	3 mg/kg body weight dissolved insaline. Single dose treatment using oral gavage.
positive control	standard drug + <i>Castor oil</i> + loperamide	10 ml/kg / Through oral gavage
Test Group- 1	<i>Castor oil</i> +200 mg/kg of Methanolic extractof <i>Lantana camara</i>	200mg/kg Body Wt./ Through Oral route Dissolved in 0.9%Saline
Test Group- 2	<i>Castor oil</i> + 400 mg/kg of Methanolic extractof <i>Lantana camara</i>	400mg/kg Body Wt. /Through Oral route Dissolved in 0.9%Saline
Test Group- 3	<i>Castor oil</i> + 200 mg/kg of Methanolic extractof <i>Myrtuscommunis</i>	200mg/kg Body Wt. /ThroughOral route Dissolved in 0.9% Saline
Test Group- 4	<i>Castor oil</i> +400 mg/kg of <i>Methanolic extract ofMyrtuscommunis</i>	400mg/kg Body Wt. / Through Oral route Dissolved in 0.9%Saline

Hereafter, the animals were constantly observed for a phase of 4 hours the following parameters determined

1. The onset of diarrhea,
2. Frequency of defecation, and
3. The weight of fecal output (wet and total feces in gram) was measured for each and every mouse.
4. The % of diarrheal inhibition and weight of fecal output were determined based on the respective formulae.

$$\% \text{ inhibition} = (\text{Average number of WFC} - \text{Average number of WFT} / \text{Average number of WFC}) \times 100$$

Where,

WFC=wet feces in the control

WFT=wet feces in the test group.

Percentage of wet fecal output = (Mean weight of wet feces of each group/ Mean weight of wet feces of control) x 100

Percentage of total fecal output = (Mean weight of total feces of each group/ Mean weight of total feces of control) x 100

The in vivo antidiarrheal index (ADI) for the plants extracts and standard drug was determined by means of employing the following formula:

$$ADI = \sqrt[3]{(Dfreq \times Gmeq \times Pfreq)}$$

Dfreq= (Mean onset of diarrhea in treated group-Mean onset of diarrhea in negative control/Mean onset of diarrhea in the negative control group) x 100

### Statistical Analysis

All the results were articulated as Mean  $\pm$  S.E.M. The inter group disparity amongst the various groups was analyzed by means of one way analysis of variance (ANOVA) using the Graph Pad Prism, version 5.0. Results were taken as statistically significant when  $p < 0.05$ .

## RESULTS

### Percentage yield of Methanol extract of *Myrtuscommunis* and *Lantana camara*

**Table 2: Percentage yields of extracts**

S no	Solvent	Percentage Yield
1.	<i>Myrtuscommunis</i>	12.27%
2.	<i>Lantana camara</i>	11.43%

Phytochemical ingredient present in Methanol extract of *Myrtuscommunis* and *Lantanacamara*

**Table 3: Particulars of qualitative phytochemical assessment of methanol extract of selected plants.**

S.No.	Phytochemical Constituent	Tests	<i>Myrtuscommunis</i>	<i>Lantana camara</i>
1	<b>Alkaloids</b>			
		Mayer's test	+	+
		Wagner's test	+	+
2	<b>Carbohydrates</b>			
		Molisch's test	+	+
3	<b>Reducing Sugars</b>			
		Fehling's Test	+	-
		Benedicts test	+	-
4	<b>Saponins</b>			
		Foam test	+	+
		Haemolysis test	+	+
5	<b>Flavones and Flavonoids</b>			
		Caddy's test	+	+
		Shinoda test	+	+
6	<b>Phenols</b>			
		Ferric chloride test	+	-
		Lead acetate test	-	-
7	<b>Tannins</b>			
		Ferric chloride test	+	-
8	<b>Flavonoids</b>			
		Lead acetate test	-	-
		Alkaline reagent test	-	-
9	<b>Glycosides</b>			
		Borntrager's test	+	+
		Legals test	+	+
10	<b>Proteins &amp; Amino acids</b>			
		Biuret test	-	-
		Ninhydrin test	-	-
11	<b>Triterpenoids</b>			
		Tin+thionyl chloride	-	-
12	<b>Fixed oils &amp; fats</b>			
		Spot test	-	-
		Saponification test	-	-

The strapping presence of needed phytochemicals in Methanol extract was witnessed. And additional investigations, extracts of *Myrtuscommunis* and *Lantana camara* were carried out.

#### Toxicity study

In the current exploration, the Methanol extracts of *Myrtuscommunis* and *Lantana camara* were relieved for studies of acute toxicity. For the determination of LD50 dose, Methanol extract of *Myrtuscommunis* and *Lantana camara* was given up to dose of 2 gm/kg b.w. and extracts did not exhibited any sort of mortality, that's why 1/5<sup>th</sup> (400mg), 1/10<sup>th</sup> (200mg) of utmost dose given were preferred for the current investigation.



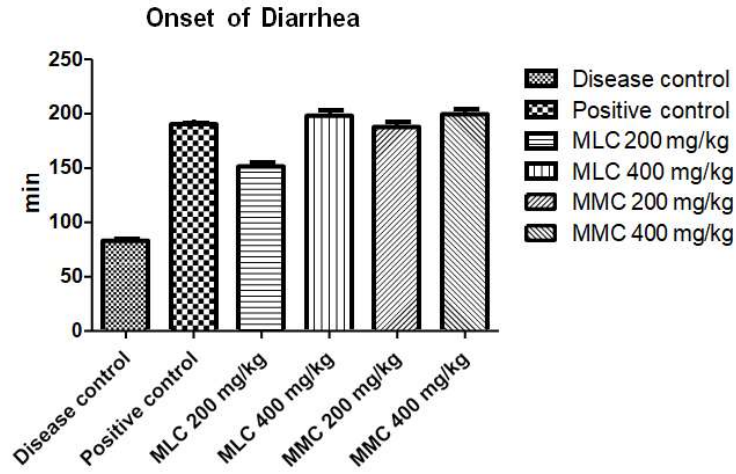


Fig 1: Onset of Diarrhea

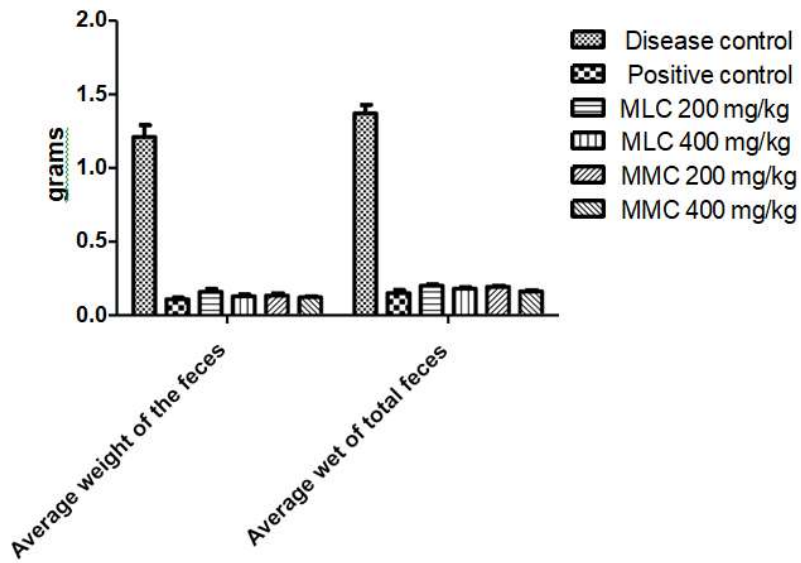


Fig 2: Avg. wt of Faces Vs Total Avg. wt.

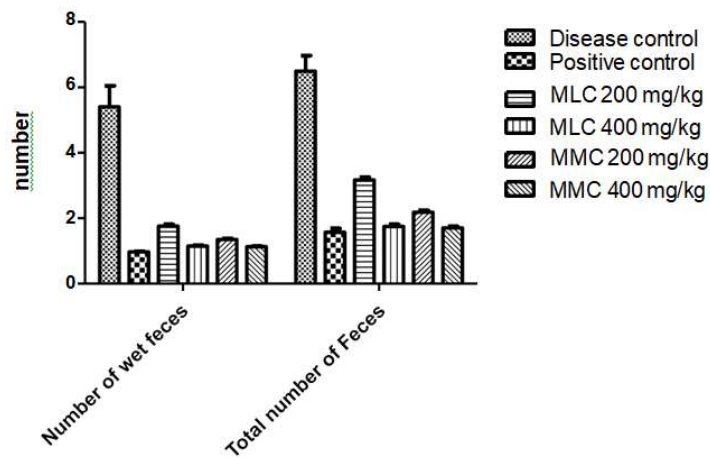
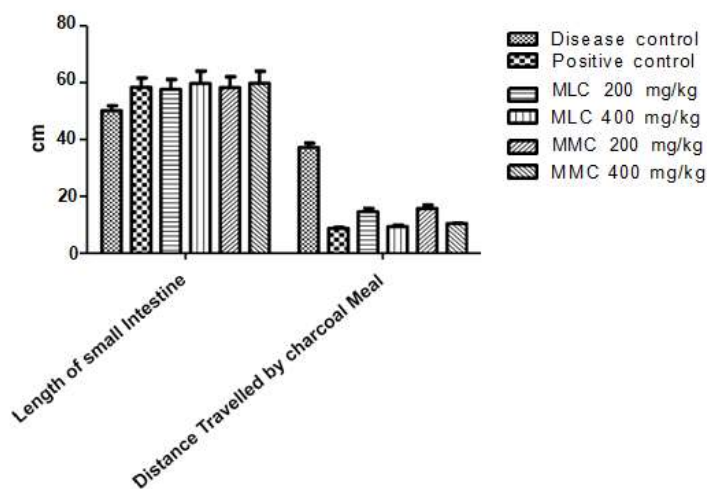


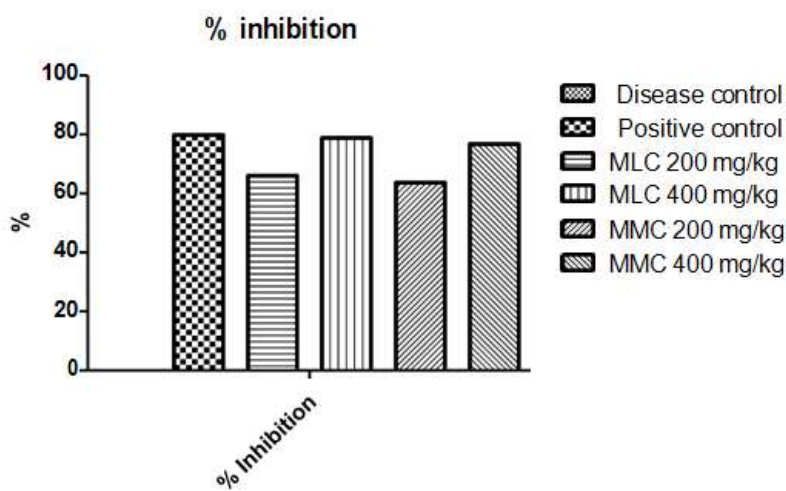
Fig 3: Wet feces Vs Number

**Table 6: Gastrointestinal Transit**

Group name	Length of small Intestine (cm)	Distance Travelled by charcoal Meal (cm)	Peristaltic Index (%)	% Inhibition
Disease control	50.14 ± 1.78	37.22 ± 1.47	74.23 ± 3.18	-
positive control	58.45 ± 3.25	8.74 ± 0.36	14.95 ± 0.32	79.85
Test Group- 1	57.72 ± 3.47	14.62 ± 1.12	25.19 ± 0.48	66.06
Test Group- 2	59.76 ± 4.35	9.38 ± 0.46	15.69 ± 0.26	78.86
Test Group- 3	58.32 ± 3.75	15.75 ± 1.23	27 ± 0.35	63.72
Test Group- 4	59.83 ± 4.22	10.31 ± 0.37	17.23 ± 0.41	76.78



**Fig 4: Gastrointestinal Transit**



**Fig 5: Percentage Inhibition**

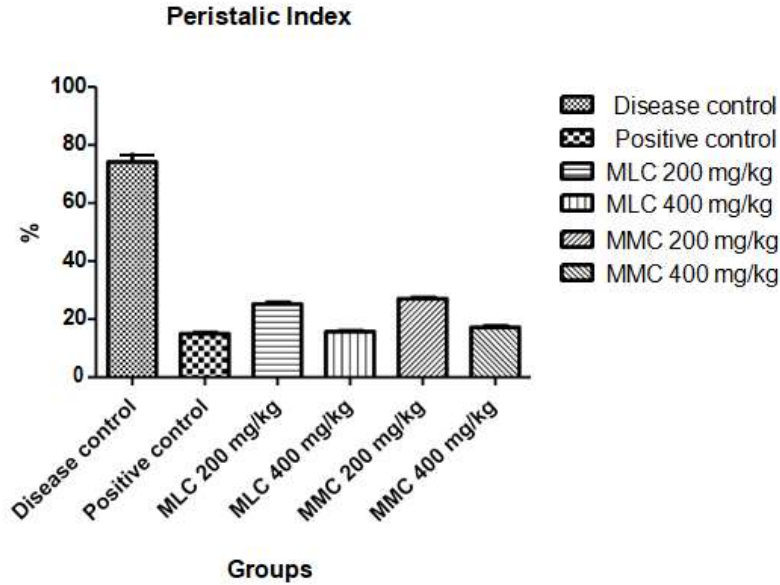


Fig 6: Peristaltic Index

Table 7: Antidiarrheal Index

Group name	Delay in Defecation (Time of Onset in min, Dfreq) (%)	Gut Meal Travel Distance (Gmeq)(%)	Purging Frequency in Number of Wet Stool (%)	Antidiarrheal Index
Disease control	-	-	-	-
positive control	129.43	81.17	81.86	95.02
Test Group-1	127.14	72.45	74.83	88.13
Test Group-2	139.98	79.16	78.26	94.78
Test Group-3	126.89	71.94	74.37	87.84
Test Group-4	139.24	78.86	77.84	94.25

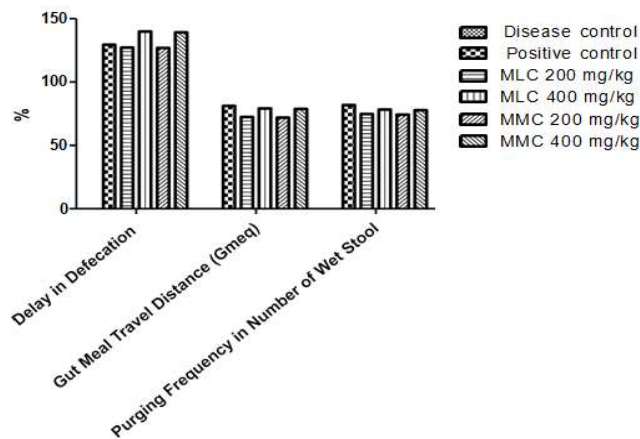


Fig 7: Purging Frequency in Number of wet stool



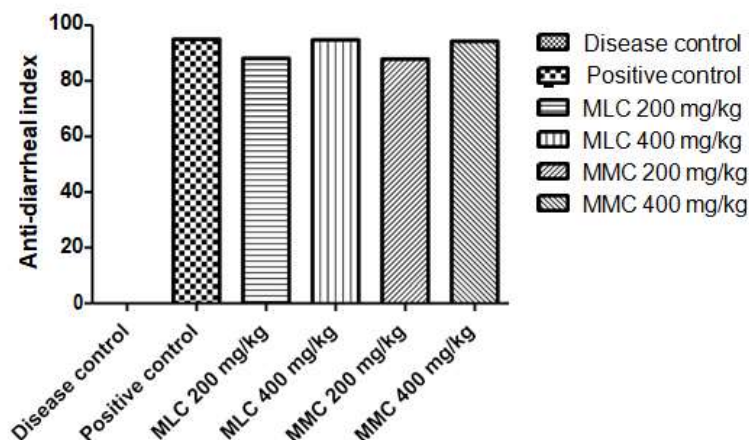


Fig 8: Anti-Diarrheal Index

## DISCUSSION

People usually use diverse parts of the plant for the treatment of a variety of ailments, include diarrheal disease without any scientific foundation regarding their safety and efficacy. yet, a variety of studies have been undertaken to authenticate the utilize of anti-diarrheal actions of medicinal plants by means of investigating the biological action of extracts of the plants have anti-spasmodic property, impediment intestinal transit, suppress motility of gut, rouse water absorption, or diminish the intraluminal accumulation fluid<sup>101</sup>. in addition, the study conducted on the extract of *Myrtus communis* and *Lantana camara* established antidiarrheal actions against castor oil-induced diarrhea in dropping the frequency of defecation in mice. Hence, this study was intended to assess the antidiarrheal activity of the *Myrtus communis* and *Lantana camara* by means of Swiss albino mice models against castor oil stimulated diarrhea, castor oil stimulated gastrointestinal transit, and castor oil stimulated accumulation of gastrointestinal fluid as contrast with the preceding study. Diarrheal disease is illustrated by means of recurrent defecation of feces of little consistency, might be due to a disorder in the move of electrolytes and water in the intestines. although there are numerous causes for diarrheal disease, the 4 main mechanisms behind the pathophysiology of diarrheas are osmotic diarrhea is caused by means of augment in intraluminal osmolarity and diminish in water absorption; secretory diarrhea, which augment the electrolyte secretion; unbalanced motility of intestinal causing a drop off transit time<sup>102-103</sup>; and inflammatory and infectious diarrhea, caused by disturbance of the epithelium of the intestine owing to pathogens like viral, bacterial, or protozoal and the immune reaction to inflammatory circumstances in the bowels<sup>104-105</sup>. In the execution of antimotility, diarrhea, and anti-secretory agent are seem to be the chief stay agents utilized to drop off the pathophysiologic circumstances accountable for the progress of diarrhea<sup>106</sup>. Castor oil has been considerably utilized for the induction of diarrhea in antidiarrheal investigations since it discharge ricinoleic acid, a metabolite that produce diarrhea<sup>107</sup>. Ricinoleic acid start diarrhea through mechanisms that consist of inflammation of gastrointestinal mucosa, resulting to the release of prostaglandin rouse gastrointestinal motility and electrolyte emission, lessen absorption of electrolyte from the intestine and colon, a mechanism that is much similar to the pathophysiologic technique resultant in diarrhea<sup>108</sup>. Prostaglandins of the E series are very recognized to have diarrheagenic properties in experimental animals along with in human beings. Consequently, the inhibitors of biosynthesis of prostaglandin are considered to impediment diarrhea induced by castor oil induced<sup>109</sup>. And the standard antidiarrheal drug, loperamide, utilized for the disease control is a synthetic opiate agonist stimulates them opioid receptors in the massive gut myenteric plexus. Those receptors are situated pre-synaptically on the ending of the parasympathetic cholinergic innervations of the smooth muscle of intestine exert a facilitatory action on contractility of clean muscle. Stimulation of receptors of m-opioid via loperamide inhibits the discharge of acetylcholine and consequently calm down smooth muscle tone within the wall of intestine<sup>110</sup>. These physiologic final consequences augment phasic colonic segmentation and slow down peristalsis, therefore rising intestinal transit time<sup>111</sup>. The inhibitory force of loperamide on acetylcholine cause inhibition of discharge intervened with acetylcholine. As a outcome, loperamide lessen every day fecal volume, reduce fluid and loss of electrolyte, and may perhaps augment viscosity of stool and bulk density. Coming to the *Myrtus communis* and *Lantana camara*, the result of the study verified that the plant extracts was caused a noteworthy impediment in the onset of diarrhea, reduction in the occurrence of output of wet fecal and total fecal, along with diminish in the mean weight of wet feces and output of total fecal that were caused by means of castor oil. In addition, the percentage inhibition of defecation, weight of output of wet feces and the total weight of

output of feces were observed in a dose-dependent way the maximum percent of inhibition was seen at 400 mg/kg dose of the plant extracts. This designated that the elevated dose of the plant extracts is allied with an enhanced antidiarrheal produce is comparable with the standard antidiarrheal medicament loperamide. This may perhaps involve that the components of the plant extract are accountable for antidiarrheal effects are more probable to be intense in the elevated doses of the plant extractions this may perhaps designate that a comparatively elevated dose of the plant extracts is required to produce a marked antidiarrheal effect. These outcomes are in agreement with information's from studies carried out on other species of medicinal plants<sup>112</sup>. Moreover, these consequences are also in line with the result of the preceding study carried out on the root of *Myrtus communis* and *Lantana camara* in aspects of percentage defense of defecation<sup>113</sup>. In relation to castor oil-induced motility of gastrointestinal, the medicinal plant extracts appreciably ( $P < .05$ ) inhibited the propulsive movement of charcoal marker at the two test doses on the distance moved by means of charcoal meal as comparison with the disease control group. In addition at all dose ranges employed, the medicinal plant extracts was capable to considerably ( $P < .001$ ) inhibit gastrointestinal fluid buildup. On the other hand, the medicinal plant extracts also exposed significant ( $P < .01$ ) lessening in the weight of contents of intestine at all test doses employed in the investigation. This may designate that the medicinal plant extracts has antisecretory action abridged an excessive discharge arbitrated through irritant actions of ricinoleic acid, a castor oil metabolite. It is extensively reported that diverse antidiarrheal agents show their actions through diverse mechanisms like inhibiting discharge, declining motility, impeding intestinal transit, dropping accumulation of intraluminal fluid or by means of improving water absorption<sup>113</sup>. further, the medicinal plants has reported to showing anti-inflammatory and analgesic actions that may perhaps be allied to inhibition of biosynthesis of prostaglandin and this in turns guide to inhibition of castor oil regulated diarrhea through inhibition of prostaglandin generation. Although additional studies are necessary, this might perhaps point out a potential antidiarrheal action of the medicinal plant extracts in opposition to diarrhea induced by means of susceptible infective agents. Furthermore, the antidiarrheal effect of *Myrtus communis* and *Lantana camara* extracts is additionally strengthened by the in vivo ADI value of medicinal plant extracts measures amount of the plant extracts is efficient in the diarrhea management. the other investigation established that the elevated the ADI value, the superior is the efficiency of the extract in the action of diarrhea. Consequently, the ADI value augmented in a dose-dependent way, the ADI of the advanced dose of the plant extracts is similar to that of the loperamide, standard drug. This may perhaps specify that the plants have a potential antidiarrheal action, may perhaps provide as a template in the progress of a novel antidiarrheal drugs. additionally, numerous variety of the literature established that plants possessing saponins, steroids, alkaloids, flavonoids, and tannins had been account to elicit antidiarrheal action due to their antispasmodic influence on the gastrointestinal tract<sup>114</sup> and anti-secretory actions<sup>115</sup>. Flavonoids have an capability to inhibit motility of intestinal and hydro-electrolytic discharges and tannins causes precipitation of proteins, dropping secretion and peristaltic movements<sup>116</sup>. In adding up, tannin produces relaxation of muscle by means of declining the intracellular  $Ca^{2+}$  inward current or through activation of the system of calcium pumping<sup>117</sup>. information from literature also demonstrated that tannins possess an antispasmodic and muscle relaxant activity, flavonoids inhibit prostaglandin E<sub>2</sub>-induced intestinal discharge, saponins inhibit histamine discharge, terpenoids inhibit the liberate of prostaglandins, and phenols lessen intestinal secretion and transit and possess an astringent effect. All these events lead to the inhibition of diarrhea by lessening intestinal secretion and motility. Most of the secondary metabolites were noticed in extracts of *Myrtus communis* and *Lantana camara*. although the definite mechanism of action of the medicinal plant has not yet recognized, the antidiarrheal effect of the plant extracts may perhaps be produced by means of these chemical constituents contribute to its facility to hindrance in onset of diarrhea, anti-motility, and anti-secretory actions. With view to acute toxicity test, the plant extract was initiated to be safe as no signal of toxicity was seen in the acute oral toxicity examination at the limit dose of 2000 mg/kg in mouse. At the test dose, mortality and deferred toxicity were not seen in the 14 days post-treatment phase. On the basis of the result of the oral acute toxicity test, the LD<sub>50</sub> value of the extracts of the medicinal plants is higher than 2000 mg/kg. usually, if the LD<sub>50</sub> value of the test chemical is further than 3 times of its smallest amount effective dose, the substance is taken as a good quality candidate for additional investigation<sup>119</sup>. consequently, the finding imply that the LD<sub>50</sub> value of plant extracts is higher than three times of its minimum effective (200 mg/kg) dose, and the plant is a good candidate for auxiliary investigation. Overall, the result of oral acute toxicity test indicated that the extract of the extracts of *Myrtus communis* and *Lantana camara* tolerable and safe and sound subsequent to oral administration authenticates the safer use of the plants in traditional background.

## CONCLUSION

The study investigated the acute toxicity of the plants extracts, the plants *Myrtus communis* and *Lantana camara* are instituted to be nontoxic and its LD<sub>50</sub> is higher than 2000 mg/kg, which ensures the safe use of the plants extracts. The *Myrtus communis* and *Lantana camara* exhibited antidiarrheal effect on evaluation in animal models by means of Swiss albino mice. The plants extracts established a noteworthy delay in the onset of diarrhea, abridged the occurrence of wet feces and also endowed with noteworthy anti-secretory effects at all doses assessed

experimentally. And also, the plants extracts signified the antimotility activity at its higher doses. Though additional investigations are warranted by means of various anti-diarrheal models and solvents, at this stage the findings of the investigation established the anti-diarrheal activity of the plants.

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