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Antidiarrhoeal potentials of methanol flower-head and leaf extracts of *Spilanthes Filicaulis* in castor oil-induced Rats

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ABSTRACT:
Diarrhoea remains a prevalent and challenging health issue worldwide. Traditional medicine often employs plant extracts for treatment, yet scientific validation of their efficacy is essential. This study investigates the antidiarrhoeal potential of methanol extracts from the flower-head and leaf of *Spilanthes filicaulis* using a castor oil-induced diarrhoea model in rats. The qualitative phytochemical analysis of the extracts was conducted to identify key constituents. Adult albino mice and Wistar rats were used in this study, acclimatized for seven days, and maintained with standard feed and water. *Spilanthes filicaulis* was collected, authenticated, and its flower-heads and leaves were dried, powdered, and extracted with 80% methanol. The extracts were filtered, concentrated, and stored at 4°C. Acute toxicity was assessed in 42 mice with doses ranging from 10 to 5000 mg/kg bw, revealing no deaths. Antidiarrhoeal activity was evaluated by pretreating rats with different doses (100 mg/kg, 200 mg/kg, and 400 mg/kg) of the extracts and measuring the frequency of defecation and gastrointestinal motility. Gastrointestinal motility was measured using charcoal meal. Data were analyzed with ANOVA in SPSS, with significance at $p < 0.05$. The phytochemical analysis revealed the presence of flavonoids, tannins, glycosides, saponins, and other compounds in both extracts, with higher concentrations in the leaf extract. The acute toxicity test indicated no fatalities, suggesting safety up to 5000 mg/kg bw. In the antidiarrhoeal assay, the flower-head extract exhibited greater efficacy with a maximum inhibition of 73.91% compared to 30.43% for the leaf extract. Gastrointestinal motility tests showed that the extracts could modulate transit, though the changes were not statistically significant across all doses. The methanol extracts of *Spilanthes filicaulis* flower-head and leaf demonstrate significant antidiarrhoeal activity, with the flower-head extract showing superior efficacy. The study supports the potential of these extracts as natural remedies for diarrhoea and underscores the need for further research to confirm their clinical benefits and mechanisms of action.

Keywords: Spilanthes filicaulis, methanol extract, antidiarrhoeal, castor oil-induced diarrhoea, gastrointestinal motility

1. INTRODUCTION:

Diarrhoea is still a major global health concern, especially in the 3rd world countries due to high incidences of morbidity and mortality (World Health Organization [WHO], 2024). Diarrhoea is a major health concern in man and animals and ranks highly as a cause of death in persons in the three world especially in the third world countries. Diarrhoea is still one of the most rampant diseases which many governments and international organizations have tried to reduce. Every year diarrhoea alone kills more than five million to eight million children less than five years old (Fauci et al., 1993).

In animals, the disease is most common in the first two weeks of life and varies in frequency from herd to herd. MA-However, cases of explosive outbreaks of diarrhoea can be major killers in some years (Greenwood et al. , 2007). Diarrhoea is a change in bowel habit that involves excessive bowel sounds, frequent passage of stool, soft and loose stool and abdominal pain (Guerrant et al. , 2001). In clinical sense it is used to refer to increased stool, General characterized by enhanced stool weight and frequency Suleiman et al. , (2008). Diarrhoea is an acute manifestation of viral, bacterial, parasitic, protozoan infection, nutritional disorder, or poisoning (Susan and Asa, 1998). In acute diarrhea there is loss of body fluids and electrolytes, which leads to dehydration, circulatory shock and death whereas in sub-acute diarrhea the condition persists for several days with malnutrition and emaciation being the common outcomes (Greene, 2006).

The most widely used antidiarrhoeal drugs often have drawbacks or side effects for example, the development

of tolerance to loperamide and diphenoxylate, urinary retention, gastric atony, and intestinal ileus with atropine (Barar, 2005). Similarly, the use of multiple drugs like antacids, anticholinergics, analgesics, protectants, antibiotics and anti-inflammatory drugs in the chemotherapeutic approach to diarrhoea is not only expensive but may also decrease the absorption and the bioavailability of other drugs. Given that anti-diarrhoeal drugs are seldom effective, the WHO encouraged the use of herbs as a form of medication (Ode et al. , 2013).

Medicinal plants occupy central position in traditional system of medicines. It has been estimated that between 25 to 50% of current drugs originate from plant sources. Because diarrhea is a common ailment throughout human development stages ad exists frequently in communities, plants play a vital role in managing diarrhea. Herbal and conventional medicines have been advocated for their effectiveness and fewer side effects as compared to those synthetic ones (Balestracci et al, 2023). Of these, Spilanthes filicaulis (A. Rich), which belongs to the Asteraceae family of plants, has been used to establish its antidiarrhoeal potential.

The species Spilanthes filicaulis is a creeping plant of tropical regions and belongs to the family asteraceae (formerly known as compositae) are widely used in folk medicine as well aromatic seasoning in foods (Christophe, 2006). undefined has been recently targeted as many claims associated with its medicinal value. Several articles have demonstrated that the extracts, formulations, and bioactive compounds of Spilanthes filicaulis have applications in various fields in the pharmaceutical and cosmetics industries. Spilanthes extracts have uses in pharmaceuticals as tooth aching formulations, for pain, inflammation, and gum infections and in mouth washes. As Vogel (2013) postulated, the major phytochemicals located there in are alkylamiden, alkaloids, terpenoids and flavonoids.

Spilanthes filicaulis is known for its diverse phytochemical profile, which includes alkaloids, glycosides, flavonoids, carbohydrates, tannins, phenolics, saponins, terpenoids, and steroids (Ojo et al, 2024). The presence of these phytochemicals is believed to contribute to its therapeutic properties. For instance, flavonoids and phenolics are recognized for their antioxidant and anti-inflammatory properties, which could play a role in mitigating diarrhoeal symptoms (Afroz et al, 2024). Methanol extracts of both the flower-head and leaves of *Spilanthes filicaulis* exhibit substantial amounts of these bioactive compounds, which may underlie their medicinal efficacy (Beserra et al, 2016).

The antidiarrhoeal activity of plant extracts often involves modulation of gastrointestinal motility and secretion. In a study by Ojo et al, (2023), the methanol extracts of *Spilanthes filicaulis* were evaluated using the castor oil-induced diarrhoea model in rats. Castor oil induces diarrhoea by converting ricinoleic acid into its active form, which stimulates intestinal motility and secretion (Salimon, 2018; Ani, Omenyi & Achebe, 2015). The extracts of *Spilanthes filicaulis* have been shown to significantly reduce the frequency of defecation in this model, suggesting their potential to alter gastrointestinal motility and secretion.

In comparative studies, the methanol extract of *Spilanthes filicaulis* flower-head has shown notable antidiarrhoeal effects when compared to the leaf extract. For example, in a study by Sharma et al, 2015), the flower-head extract at various dosages (100, 200, and 400 mg/kg) significantly reduced the frequency of antidiarrheal activity of ethanolic extract of Holarrhena antidysenterica seeds in rats. The leaf extract also demonstrated efficacy, but the flower-head extract appeared more potent, particularly at higher doses (400 mg/kg). The relative efficacy of these extracts could be attributed to their distinct phytochemical compositions and concentrations of active compounds.

The pharmacological evaluation of these extracts involves assessing parameters such as the frequency of defecation and the percentage of inhibition of castor oil-induced diarrhoea. For instance, in a controlled study, the flower-head extract demonstrated a maximum inhibition of 73.91%, while the leaf extract showed a maximum inhibition of 30.43% at equivalent dosages (Yuan et al, 2020; Ani, Omenyi, & Nwigbo, 2015). These findings underscore the potential of *Spilanthes filicaulis* flower-head extract as a more effective antidiarrhoeal agent compared to the leaf extract. However, both extracts exhibited dose-dependent effects, indicating that higher doses generally provide better therapeutic outcomes.

The study on the antidiarrhoeal potentials of methanol extracts of *Spilanthes filicaulis* flower-head and leaf is critical due to the global prevalence of diarrhoeal diseases, which remain a major health issue, particularly in developing regions (World Health Organization [WHO], 2024). Despite the availability of various antidiarrhoeal medications, there is a continuous need for effective, safe, and affordable treatments. Traditional medicinal plants like *Spilanthes filicaulis* offer promising alternatives, yet their therapeutic potentials are not fully explored or validated in contemporary research. Previous studies highlight the antidiarrhoeal effects of other plant extracts, but specific research on *Spilanthes filicaulis* is limited (Ojo et al, 2023; Ani, Ani, & Chukwuneke, 2015). The methanol extracts of *Spilanthes filicaulis* flower-head and leaf have shown potential in preliminary investigations, but comprehensive studies are lacking. For instance, while some research has documented the antidiarrhoeal activity of related species, there is a gap in detailed evaluations of *Spilanthes filicaulis* using established models like castor oil-induced diarrhoea. Addressing this

gap could validate the use of *Spilanthes filicaulis* extracts and provide an effective natural remedy for diarrhoea.

2. MATERIALS AND METHODS:

2.1 Study Animals:

Albino mice of about 6 weeks old and Wistar albino rats of 8 weeks old were sourced from animal house of department of Zoology and Environmental Biology, University of Nigeria, Nsukka, Nigeria. The mice and rats used in this study were procured from the University's Animal house and they were habituated to the standard environmental conditions for 7 days, they were fed with regular feed and clean water.

2.2 Plant materials

A substantial amount (2736 g) of Spilanthes filicaulis was gathered from the settlement of Isuofia. Taxonomist Mr. Alfred Ozioko of the International Centre for Ethnomedicine and Drug Development in Nsukka, Enugu state, Nigeria, verified the authenticity of the plant specimen. InterCEDD/16291 is the plant's InterCEDD voucher number. Different flower heads and leaves were chosen from the plant, dried for several days at room temperature, and then ground into a fine powder. An 80% methanol extraction was performed on pulverized powdered Spilanthes filicaulis leaf and flower head, respectively. Using Whatman No. 1 filter paper, the resultant liquid extracts were filtered, and the wastes were disposed of. Prior to usage, the methanol extracts were kept at 40^0C after being concentrated in a water bath at 450 ^{0}C.

2.3 Chemicals

Castor oil (Amman., Jordan), Charcoal meal (Acuro Organics, New Delhi), Methanol, Loperamide (Imodium), atropine and castor oil (Bell, Sons and co., Druggist Ltd., Southport, England)

2.4 Phytochemical Qualitative Analysis

Test for flavonoids, tannins, carbohydrate, glycosides, saponins, steroids, terpenoids and alkaloids were carried out using standard method (Harborne, 1973; Trease and Evans, 1989).

2.5 Acute Toxicity Studies

Lethal median dose (LD_{50}) determination: Both phase 1 and phase 2 acute toxicity tests were done according to the method of Lorke (1983) using 42 mice. Twenty one mice each for MESF leaf and flower-head as shown in Table 1:

Table 1: Experimental Design and Observations for Lethal Dose Determination in Mice

Phase	Group	Number of Mice	Dosage (mg/kg bw)	No. of Deaths Recorded	Observations
Phase 1	Group 1	3	10		Observed for any death
	Group 2	3	100		
	Group 3	3	500		
Phase 2	Group 1	3	1000		Observed for any death
	Group 2	3	3000		
	Group 3	3	5000		
	Group 4	3	Normal saline (5ml/kg bw)		Observed for any death

Note: The lethal median dose was then computed based on the observed data.

2.6 Anti Diarrhoea Test:

Castor Oil-Induced Diarrhoea Test: The antidiarrhoeal effect of the methanol extract of Spilanthes filicaulis flower-head and its leaf was determined by employing the method used by Teke et al. (2007) with slight alteration. Therefore, this study used thirty-two adult albino rats of either sex that were fasted for about 22 hours. These were initially tagged, weighed and then divided into equal groups of four rats in eight (8) groups (I - viii).

Table 2: Treatment Groups and Dosages for the Experiment

Group	Treatment	Dosage	Administration Route
Group 1	Normal saline	0.2 ml	Oral
Group 2	Loperamide	2 mg/kg	Oral
Group 3	Extract of S. filicaulis leaf	100 mg/kg bw	Oral
Group 4	Extract of S. filicaulis leaf	200 mg/kg bw	Oral
Group 5	Extract of S. filicaulis leaf	400 mg/kg bw	Oral
Group 6	Extract of S. filicaulis flower-head	100 mg/kg bw	Oral
Group 7	Extract of S. filicaulis flower-head	200 mg/kg bw	Oral
Group 8	Extract of S. filicaulis flower-head	400 mg/kg bw	Oral

Before the experiment, the animals were pre-treated with saline solution; one hour later castor oil was administrated orally per animal. Faeces and the rate of defaecation were monitored in terms of regularity among the rats. Poo was obtained by placing white sheets of paper beneath individual cages and then scooping the feces. Wet and dry faecal droppings were determined by counting the number for every one hour up to four hours with a change of the white paper for each assessment. This was determined by finding the percentage inhibition (%) of the wetness of the feaces and frequency of stooling due to extract in comparison to the control group using the formula:

$$Inhibition\ of\ defaecation\ (\%) = \frac{\text{Mean No. of faeces of Control} - \text{Mean No. from treated group}}{\text{Mean No. of faeces of Control}} \times 100\%$$

Gastro-Intestinal Motility Test:

To determine the effect of the methanol extract of Spilanthes filicaulis flower-head and leaf on gastro-intestinal motility, the method developed by Mascolo et al. (1993) was applied. Thirty-two adult Wistar rats of either sex were selected and allowed to fast for 18 h. The animals were ear marked, weighed and divided into eight groups of four rats each. The diarrheal agent, castor oil, was administered orally to each rat at a dose of 1 ml. After one hour, rats in group one (control) received normal saline (0. 2ml). Group 2 was intraperitoneally injected with atropine sulphate which was equivalent to 3 mg/kg of the standard drug. Group three, four and five received 100, 200 and 400 mg/kg body weight of methanol extract of Spilanthes filicaulis leaf respectively through oral gavage. Groups 6, 7 and 8 were orally dosed with 100, 200 and 400mg/kg bw of methanol extract of Spilanthes filicaulis flower-head. After 1 hour of the above treatments, each group was administrated with 0. 2 ml of charcoal meal (0. 5 ml of 10% charcoal and the remainder was 5% gum acacia). After one hour, chloroform was administered to each rat where it was followed by sacrificial cutting on the abdomen and of the small intestine freed from the mesentrum in order to prevent mechanical stretch. The extent of the intestine from the pyloric sphincter (pylorus) to the ileo-caecal junction (caecum) and the distance covered by the charcoal meal for each rat was determined. The gastro-intestinal transit was estimated for each rat by determined the proportion of the charcoal meal that traveled a given distance of the intestinal tract.

2.7 Statistical Analysis:

Acceptable data expression for all the data was Mean ± SD. Utilizing analysis of variance (ANOVA) to evaluate for significance at $p < 0.05$, the data were examined using the Statistical Package for Social Sciences (SPSS) version 20 for Windows. The mean of each group following each treatment was compared to the controls, with a significance level of $p < 0.05$ indicated.

3. RESULTS:

3.1 **Qualitative analysis of phytochemical constituents**

Qualitative analysis carried out showed the presence of important phytochemical constituents as summarized in Table 1.

Table 1: Phytochemical Constituents in *Spilanthes filicaulis*

Phytochemical Constituent	Relative Amount (Leaves)	Relative Amount (Flower-Head)
Alkaloids	-	-
Glycosides	++	++
Flavonoids	++	+
Carbohydrates	+++	+
Tannins	+++	++
Total Phenolics	+++	++
Saponins	+++	++
Terpenoids	+++	+
Steroids	+++	+

Data represented as Mean ± SD (n = 3); + = Present in trace amount; ++ = Present in moderate amount; +++ = Present in large amount; - = Not Detected

3.2 Acute Toxicity Test:
The acute toxicity test shows that between 10 mg/kg bw and 5000 mg/kg bw no death was recorded. This shows the relative safety or non-toxic nature of the extracts.

3.2.1 Effect of MESF leaf and Flower-Head on Castor Oil-Induced Diarrhoea:
Table 2 displays the degrees of defecation inhibition generated by MESF leaf and flower-head in comparison to the control (group 1). Time and dosage depended on the pretreatment. computed mean wet droppings at the 4-hour mark. It was determined which group's percentage inhibition was higher than the control's. Group six had the lowest inhibition (-13.04%) to diarrhea, whereas group eight had the highest inhibition (73.91%). Consequently, MESF flower-head suppressed diarrhea more than MESF leaf at greater concentrations.
Table 2 presents the inhibition of castor oil-induced defecation frequency by *Spilanthes filicaulis* leaf and flower-head extracts. Group 1 (control) had a mean of 5.75 ± 2.50 wet droppings over four hours. Group 2 (Loperamide) showed significant inhibition with a mean of 1.75 ± 1.03 and 69.57% reduction. Group 3, receiving 100 mg/kg of leaf extract, had 4.00 ± 2.04 mean droppings and 30.43% inhibition. Group 4 (200 mg/kg leaf) and Group 5 (400 mg/kg leaf) showed minimal inhibition. Groups 6 to 8 with flower-head extracts showed varying efficacy, with Group 8 (400 mg/kg) achieving the highest inhibition of 73.91%.

Table 2: Inhibition of Castor-Oil Induced Frequency of Defecation by MESF Leaf and Flower-Head

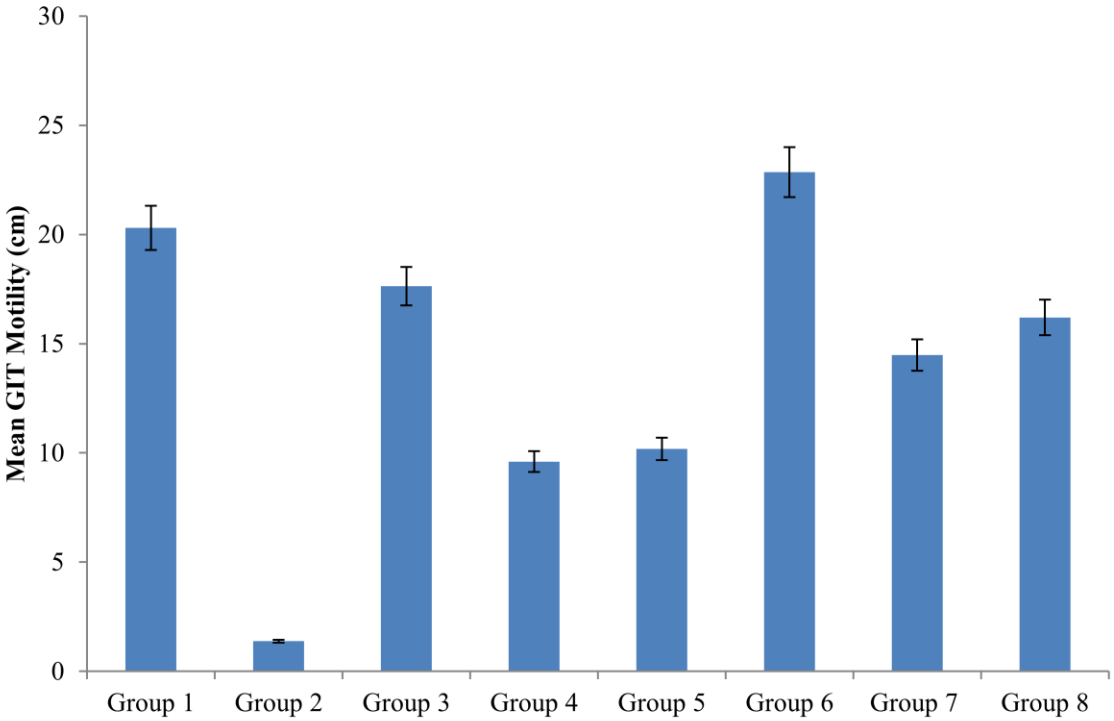
Group	Description	1 hr	2 hr	3 hr	4 hr	Mean hr (± SD)	% Inhibition
1	Normal saline + Diarrhoea (Control)	9	2	11	1	5.75 ± 2.50	-
2	2 mg/kg Loperamide + Diarrhoea (Reference)	0	0	4	3	1.75 ± 1.03	69.57
3	100 mg/kg of MESF leaf + Diarrhoea	3	10	2	1	4.00 ± 2.04	30.43
4	200 mg/kg of MESF leaf + Diarrhoea	4	13	3	3	5.75 ± 2.43	0
5	400 mg/kg of MESF leaf + Diarrhoea	7	9	0	5	5.25 ± 1.93	8.7
6	100 mg/kg of MESF flower-	5	12	9	0	6.50 ± 2.60	-13.04

	head + Diarrhoea						
7	200 mg/kg of MESF flower-head + Diarrhoea	0	9	5	0	3.50 ± 2.18	39.13
8	400 mg/kg of MESF flower-head + Diarrhoea	0	4	1	1	1.50 ± 0.87	73.91

Data represented as Mean ± SD (n = 3)

3.2.2 Effect of MESF Leaf and Flower-Head on Gastro Intestinal Motility.

Using charcoal meal as a marker, Figure 1 illustrates how the extracts affect the gastrointestinal motility of Wistar albino rats. The distance covered by the charcoal meal was significantly reduced ($p < 0.05$) in group two (reference). Comparing the distance traveled by the charcoal meal an hour later to group one (control), groups three, four, five, seven, and eight showed no significant decrease ($p > 0.05$), while group six showed no significant increase ($p > 0.05$). Therefore, the rats' gastrointestinal motility was slightly but not significantly altered by the extracts. As a control, Group 1 received 0.2 milliliters of charcoal meal and normal saline to cause diarrhea. Groups 3 to 5 were administered MESF leaf extract at escalating doses (100, 200, and 400 mg/kg), with Group 2 receiving 2 mg/kg atropine as a comparison. MESF flower-head extract at doses of 100, 200, and 400 mg/kg was given to groups 6 through 8. The charcoal meal's travel distance is represented by a bar chart that shows the various impacts of these treatments on gastrointestinal motility.



Group 1 = Diarrhoea + Normal saline + 0.2 ml charcoal meal (Control).
Group 2 = Diarrhoea + 2 mg/kg Atropine + charcoal meal (Reference)
Group 3 = Diarrhoea + 100 mg/kg of MESF leaf + charcoal meal
Group 4 = Diarrhoea + 200 mg/kg of MESF leaf + charcoal meal
Group 5 = Diarrhoea + 400 mg/kg of MESF leaf + charcoal meal
Group 6 = Diarrhoea + 100 mg/kg of MESF flower-head + charcoal meal
Group 7 = Diarrhoea + 200 mg/kg of MESF flower-head + charcoal meal
Group 8 = Diarrhoea + 400 mg/kg of MESF flower-head + charcoal meal
Data represented as Mean ± SD (n = 3).

Figure 1: Bar chart showing the effect of MESF leaf and flower-head on gastro-intestinal motility of albino rats

4. DISCUSSION:

Methanol extract of *Spilanthes filicaulis* flower-head and leaf used by traditional medicine practitioners were analyzed to evaluate their phytochemical constituents, antioxidant activity, antidiarrhea and toxicologic properties. Results on Table 1, show the presence of flavonoid, tannins, glycoside, carbohydrates, saponin, phenolics, terpenoids and steroids in the plant part extract. These phytochemicals were found to be higher in the leaf extracts than in the flower-head extract. These phytochemicals could be responsible for antiscorbutic, diuretic, anaesthetic, antidiarrhoeal and anti-inflammatory properties associated with the plant (Ainslie, 1937; Adegoke *et al*., 1968). The two extracts appear to be nontoxic up to 5000 mg/kg bw, based on the study's median lethal dose (LD50), which did not result in any mouse deaths. Castor oil-induced diarrhoea test was used to examine the impact of methanol leaf and flower-head extract of Spilanthes filicaulis on diarrhoea (Table 2). According to the study, the flower-head extract prevented diarrhea better than the leaf extract. However, a larger dosage of the flower-head extract is needed because the lowest dose (100 mg/kg bw) showed no beneficial effects on the prevention of diarrhea. The antisecretory mechanism may have been the method by which the extracts acted to prevent diarrhea. The test groups' lower total number of wet feces in comparison to the control group is indicative of this.

Since diarrhea is known to be caused by microorganisms, plants with the ability to stop microbial growth may be able to treat diarrhea. The presence of phytoconstituents in the extracts, such as flavonoids, phenolic compounds, glycosides, and saponins, has been shown to prevent bacterial development, which may lower the frequency and quantity of wet stools. In the gastro-intestinal motility test, activated charcoal was utilized to determine the impact of methanol leaf and flower-head extract of Spilanthes filicaulis on peristaltic movement. According to studies on activated charcoal, substances like pharmaceuticals and chemicals are absorbed by the charcoal particles' surface, which prevents absorption (Omoboyowa et al., 2013). The result (Figure 1) has revealed that the leaf extract and the flower-head extract has delayed the gastro-intestinal motility and the propulsion of charcoal meal in both the 200 and 400 mg/kg bw. The inhibition of the propulsion of charcoal meal through the gastro intestinal tract could also have been due to pre-treatment with Spilanthes filicaulis leaf and flower-head. Gastrointestinal transit time was observed to have increased and that more time has been provided for the reabsorption of water content from the faeces which may have helped contribute to the reduced watery consistency of the faecal matter (Omoboyowa et al . , 2013). This could be due to phenolics like tannins and flavonoids that act by competing with histamine and acetylcholine that cause contraction of the gut. It has been proposed that the Castor oil induced gastrointestinal motility is cholinergically induced as this can be blocked by atropine, an anti-cholinergic agent (Brown & Taylor, 2005). In this particular experiment, atropine when used as a control reduced the distance covered by the charcoal meal preferentially.

CONCLUSION:

The study on the antidiarrhoeal potentials of methanol extracts of *Spilanthes filicaulis* flower-head and leaf provides valuable insights into their therapeutic efficacy and safety. The qualitative phytochemical analysis confirmed the presence of significant bioactive compounds in both the leaf and flower-head extracts, including flavonoids, tannins, glycosides, and saponins, which are known for their medicinal properties. The Spilanthes filicaulis extracts showed low toxic profile and moderate antidiarrhoeal properties.

The acute toxicity tests revealed that both extracts are relatively non-toxic, with no mortality observed up to 5000 mg/kg bw, underscoring their safety profile. In the castor oil-induced diarrhoea model, the methanol extracts demonstrated notable antidiarrhoeal effects. Particularly, the flower-head extract exhibited superior efficacy, achieving a maximum inhibition of 73.91% at 400 mg/kg, compared to the leaf extract's highest inhibition of 30.43% at 100 mg/kg. This suggests that the flower-head extract has a stronger antidiarrhoeal potential.

The gastrointestinal motility test indicated that both extracts could modulate gastrointestinal transit, although the effects were not statistically significant across all doses. The observed suppression in motility aligns with the reduction in diarrhoeal symptoms, suggesting that these extracts may act through mechanisms that influence gastrointestinal secretions and motility. On the whole, the findings support the potential use of *Spilanthes filicaulis* extracts as natural antidiarrhoeal agents. The flower-head extract, in particular, shows promise for further development and clinical evaluation. Future studies should focus on elucidating the exact mechanisms of action and exploring the therapeutic efficacy in clinical settings.

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