Ethics approval and consent to participate

Ethics approval for animal use was obtained from the Animal Use and Care Committee of the NVRI (Approval number–NVRI/EC/20/010). No consent approval was required for this study.

Extraction

Hydnora abyssinica

The roots were cut into smaller pieces and dried in a hot air oven at 45°C for 5 days then ground into powder. To 571 g of the pulverized roots was added 3 L of distilled water and kept in the refrigerator and allowed to extract for a period of 24 h, after which it was filtered and the filtrate dried in a hot air oven at 50°C for 2 days to obtain the dried aqueous extract as brick red solid weighing 64.0 g with a percentage yield of 11.2%.[29,30] The dried aqueous extract of *H. abyssinica* was labeled KAQ, coined from the common Hausa name, Kaushe.

Neorautanenia mitis

Tubers of *N. mitis* were cut into smaller pieces and sun dried for 3 days and further dried in a hot air oven at 45°C for 1 day. The dried material was then pulverized, and 1000 g of the powder was extracted with 4 L of distilled water and kept in the refrigerator for 24 h, after which it was filtered and the filtrate dried in a hot air oven at 50°C for 2 days to obtain the dried aqueous extract as dark brown solid weighing 65.2 g with a percentage yield of 6.5%.[29,30] The dried *N. mitis* aqueous extract was labeled ABAQ, coined from the Hausa local name Abargora.

Vitellaria paradoxa

The stem bark was cut into smaller pieces, dried in a hot air oven at 45°C for 4 days and then pulverized. To a portion of 1000 g of powdered plant material, 4 L of distilled water was added and the mixture was kept in the refrigerator for 24 h, after which it was filtered and the filtrate dried in a hot air oven at 50°C for 3 days to obtain the dried aqueous extract as light brown solid weighing 35.0 g with a percentage yield of 3.5%.[29,30] The dried aqueous extract was labeled SBAQ, coined from the English common name Shea butter.

Senna surattensis

The leaves of the plant were dried in a hot air oven at 45°C for 2 days, after which they were pulverized. To 285 g of the plant powder was added 2 L of distilled water and kept in the refrigerator and allowed to extract for a period of 24 h, after which it was filtered and the filtrate dried in the hot air oven at 50°C for 3 days to obtain the dried aqueous extract as dark green solid weighing 17.0 g with a percentage yield of 6.0%.[29,30] The dried aqueous extract of *S. surattensis* was labeled CAQ, coined from the name Cassia synonym for the genus Senna.

Preliminary phytochemical analysis

All of the aqueous extracts were subjected to a qualitative phytochemical analysis to indicate the presence or absence of specific classes of secondary metabolites, using standard methods as described by Sasidharan *et al.*[31]

Acute toxicity studies (limit test)

The acute toxicity studies were carried out using the limit test in Wister albino rats, to determine the median lethal dose (LD_{50}) of the aqueous extracts, using a standard protocol described by the Organization for Economic Co-operation and Development (OECD).[32] Briefly, three albino rats kept in separate cages were used for the testing of each extract. The first rat was given a limited dose of 2000 mg/kg of the extract orally and observed for signs of toxicity and ultimate death. If the first rat survived, the procedure was repeated with the second rat, and then the third rat if the second rat survived.

Determination of antidiarrheal activity

The four dried aqueous extracts were used for the antidiarrheal experiments, which was carried out at the Drug Development Section in the Department of Biochemistry, NVRI Vom, Nigeria.

Castor oil-induced diarrhea

For each of the aqueous extracts, 25 rats of both sexes weighing between 130 and 200 g were used for the experiments, which were conducted during the daytime. The rats were fasted for 12 h before the commencement of the experiment, having access to water only. The rats were randomly allocated into five groups of five rats each. Groups 1, 2, and 3 were given graded doses (100 mg/kg, 200 mg/kg, and 400 mg/kg) of the dried extract reconstituted in distilled water. The graded doses for the extracts were considered based on the result obtained from the toxicity studies; the doses were within safe limits for experimental purpose. Group 4 were given distilled water, while Group 5 was given loperamide. Groups 4 and 5 are the control groups. The rats were then housed singly in a perforated cage lined with white blotting paper. One h after the above treatment, all the rats in the groups were given 1 mL of castor oil orally. The rats were observed for 5 h for watery (wet) or unformed feces. The watery feces from each rat were counted hourly for up to 5 h. At the end of the experiment, the group mean feces was obtained, and the percentage of protection was calculated using the formula:[29,33]

$$\frac{\text{Mean of unformed faeces of water control} - \text{mean of unformed faeces of treatment}}{\text{Mean of unformed faeces of water control}} \times 100$$

Gastrointestinal transit of charcoal (motility test)

For each of the aqueous extracts, 25 rats of both sexes weighing between 130 and 200 g were used for the experiments, which were conducted during the day time. The animals were fasted for 16 h before the commencement of the experiment but allowed access to water. They were randomly divided into five groups of five rats each. Groups 1, 2, and 3 were treated orally with graded doses (100 mg/kg, 200 mg/kg, and 400 mg/kg) of the dried aqueous extracts reconstituted in distilled water. The graded doses for the extracts were considered based on the result obtained from the toxicity studies; the doses were within safe limits for experimental purpose. Group 4 were treated with distilled water, while Group 5 was treated with atropine sulfate. Groups 4 and 5 are the control groups. 30 min after extract and drug administrations, 1 mL of 5% activated charcoal suspension in 10% aqueous solution of acacia gum powder was given orally to each rat. After 30 min of administering the activated charcoal, the rats were humanely sacrificed and the abdomen was opened to access the intestine. The distance travelled by the charcoal meal from pylorus was measured and expressed as a percentage of the total length of intestine from pylorus to the cecum to calculate the percentage intestinal transit of activated charcoal.[34]

$$\text{Percentage of intestinal transit} = \frac{\text{Meal travel from pylorus to cecum}}{\text{Total length of small intestine from pylorus to cecum}} \times 100$$

Statistical analysis

The data were presented as mean ± standard error of mean (n = 5). Difference between means of different treatments was determined by analysis of variance using the SPSS version 23 IBM® SPSS® (NY, USA). $P < 0.05$ was considered as statistically significant.

RESULTS

The physical appearance and percentage yields obtained from the extraction procedure of all the four plants are summarized in Table 1.

Preliminary phytochemical screening

Qualitative phytochemical analysis showed the aqueous extracts of *H. abyssinica* (KAQ), *N. mitis* (ABAQ), *V. paradoxa* (SBAQ), and *S. surattensis* (CAQ) contained tannins, cardiac glycosides, steroids, and alkaloids. In addition, flavonoids were detected in all these extracts except for KAQ. Saponins were detected in KAQ, ABAQ, and CAQ but not detected in SBAQ. Anthraquinones were not detected in any of the four extracts [Table 2].

Median lethal dose (LD_{50})

No mortality was recorded in the rats treated with the limit dose of 2000 mg/kg of all the plants extracts [Table 3]. This indicates that none of the Plant has LD_{50} ≤2000 mg/kg.

Gastrointestinal transit of activated charcoal in rats treated with the aqueous crude extracts

Aqueous crude extract of Hydnora abyssinica

There was significant decrease in the intestinal transit of activated charcoal administered to rats treated with all doses of KAQ extract when compared to rats treated with distilled water [Table 4]. The rats treated with the highest dose of the extract decreased the transit to an extent comparable with the standard drug (atropine sulfate 5 mg/kg). This is an indication that the plant may have antidiarrheal activity.

Crude aqueous extract of Neorautanenia mitis

Administration of ABAQ extract did not affect the gastrointestinal transit of activated charcoal administered to rats treated with the extract when compared with the control rats treated with distilled water [Table 4]. A significant ($P < 0.05$) decrease was observed in rats treated with the standard drug (atropine sulfate 5 mg/kg) when compared to the control rats.

Aqueous crude extracts of Vitellaria paradoxa

Treatment with SBAQ did not result in significant decrease in the distance travelled by charcoal meal in the gastrointestinal tract of rats when compared to the control [Table 4]. The standard drug on the other hand significantly ($P < 0.05$) decreased the distance travelled by the charcoal meal.

Crude aqueous extract of Senna surattensis

The gastrointestinal transit of charcoal in rats treated with CAQ extract was not significantly different from the control rats. However, treatment with atropine significantly decreased intestinal transit of activated charcoal [Table 4].

Comparison of the effects of the aqueous crude extracts on intestinal transit of activated charcoal in rats

Comparison of the four extracts showed that dose-for-dose, KAQ extract significantly decreased the intestinal transit of activated charcoal when compared to the other extracts [Figure 1]. This is an indication that the KAQ extract was more effective in inhibiting gastrointestinal tract motility. Hence, this may have greater potential for antidiarrheal activity.

Inhibition of defecation after administration of the aqueous crude extracts in albino rats

Aqueous crude extract of Hydnora abyssinica

In the castor oil-induced diarrhea model, the KAQ extract significantly decreased fecal output in rats treated with the extract when compared with the control rats treated with distilled water [Table 5]. The inhibition of defecation in rats treated with 400 mg/kg (82%) was comparable to that of rats treated with the standard drug (loperamide 10 mg/kg). This is a further indication of the antidiarrheal potential of the KAQ extract.

Crude aqueous extract of Neorautanenia mitis

The fecal output of rats treated with the ABAQ extract was significantly lower than that of rats treated with distilled water. The percentage inhibition was marginally dose dependent with 100 mg/kg, 200 mg/kg, and 400 mg/kg showing 61%, 64%, and 66% inhibition of fecal output, respectively [Table 5].

Aqueous crude extracts of Vitellaria paradoxa

The mean defecation of rats treated with the SBAQ extract was significantly lower than that of rats treated with distilled water. The highest dose administered (400 mg/kg) inhibited fecal output by 32% while the lowest dose (100 mg/kg) inhibited fecal output by 13% [Table 5].

Crude aqueous extract of Senna surattensis

The fecal output of rats treated with various doses of the CAQ extract was significantly lower than that of rats treated with distilled water. The highest percentage inhibition of 81% was observed in rats treated

Table 1: Physical appearance and percentage yield of extracts from *Hydnora abyssinica, Neorautanenia mitis, Vitellaria paradoxa,* and *Senna surattensis*

Extract	Appearance	Amount of dry plant material (g)	Amount of extract (g)	Percentage yield (%)
KAQ	Brick red solid	571	64.0	11.2
ABAQ	Dark brown solid	1000	65.2	6.5
SBAQ	Light brown solid	1000	35.0	3.5
CAQ	Dark green solid	285	17.0	6.0

KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

Table 2: Phytochemical composition of *Hydnora abyssinica, Neorautanenia mitis, Vitellaria paradoxa,* and *Senna surattensis* aqueous extracts

Extract	Phytochemical composition						
	Tannins	Cardiac glycosides	Steroids	Alkaloid	Flavonoid	Anthraquinones	Saponins
KAQ	+	+	+	+	−	−	+
ABAQ	+	+	+	+	+	−	+
SBAQ	+	+	+	+	+	−	−
CAQ	+	+	+	+	+	−	+

+: Detected; −: Not detected; KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

with 400 mg/kg of the extract [Table 5]. This shows that the extract has antidiarrheal potential.

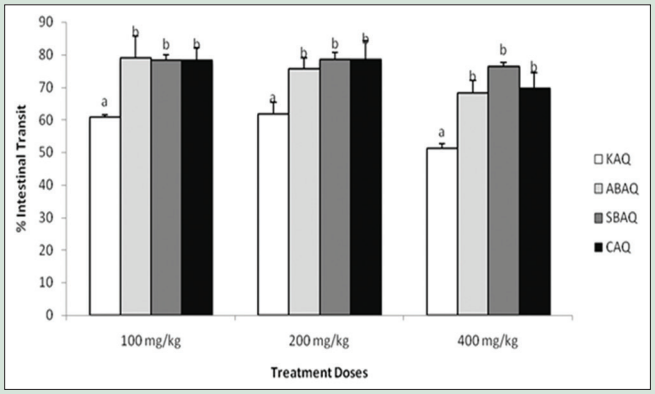

Figure 1: Comparison of intestinal transit of charcoal meal in rats treated with the different aqueous extracts. KAQ: *Hydnora abyssinica*; ABAQ: *Neorautanenia mitis*; SBAQ: *Vitellaria paradoxa*; CAQ: *Senna surattensis*. Bars with different letter superscripts in the same cluster are significantly different

Table 3: Median lethal dose of *Hydnora abyssinica, Neorautanenia mitis, Senna surattensis*, and *Vitellaria paradoxa* aqueous extracts

Extract	Number of rats	Dose (mg/kg)	Mortality	LD_{50} (mg/kg)
KAQ	3	2000	0/3	>2000
ABAQ	3	2000	0/3	>2000
SBAQ	3	2000	0/3	>2000
CAQ	3	2000	0/3	>2000

KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

Comparison of inhibition of defecation in rats treated with the aqueous crude extracts

A dose for dose comparison of the extracts showed no significant difference in the output of unformed feces of the extract-treated rats. The only exception was the significant reduction observed in defecation of rats treated with CAQ extract (400 mg/kg) when compared with SBAQ extract (400 mg/kg) [Figure 2].

When the percentage inhibition of defecation of the extracts is compared, the highest inhibition of 82% was observed in rats treated with 400 mg/kg of KAQ followed by rats treated with 400 mg/kg of CAQ (81%). The lowest inhibition at a dose of 400 mg/kg (32%) was observed in rats treated with SBAQ. At the dose of 100 mg/kg, ABAQ exhibited the highest inhibition (61%). However, on administration of higher doses (200 mg/kg and 400 mg/kg), the increase in inhibition was marginal (64% and 66%, respectively). On the other hand, inhibition of defecation in rats treated with KAQ and CAQ increased substantially with increase in dose from 200 mg/kg to 400 mg/kg [Table 6].

DISCUSSION

Phytochemicals are responsible for the biological activities of medicinal plants, and their presence in any plant extract is an indication of activity. The tannins, cardiac glycosides, steroids, alkaloids, and saponins present in *H. abyssinica* (KAQ) agrees with the findings of Wintola and Afolayan.[28] In addition, Saadabi and Ayoub[35] reported the presence of these phytochemical types with the exception of cardiac glycosides and saponins. The phytochemicals detected in *V. paradoxa* (SBAQ) were similar to those reported by El-Mahmood *et al.*[22] when various organic solvents were used for extraction. Kabila *et al.*[36] in their review on *Cassia* (synonym for Senna) species reported the presence of alkaloids, flavonoids, saponins, and tannins in either the leaf, leaf/flower, and/or aerial parts of the plant *Cassia surattensis* using various organic extraction solvents (methanol, ethanol, ethyl acetate, hexane, and chloroform).

Table 4: Percentage intestinal transit of charcoal meal in rats treated with *Hydnora abyssinica* extract, *Neorautanenia mitis* extract, *Vitellaria paradoxa* extract, and *Senna surattensis* extract

Treatment	Total length of intestine (cm)	Distance travelled by charcoal meal (cm)	Percentage intestinal transit
KAQ extract			
Water	103.28±3.87	75.30±1.30	73.36±3.26
100 mg/kg	114.56±4.07	69.66±3.05	60.75±0.76*
200 mg/kg	102.88±4.24	63.38±4.00	61.87±3.58*
400 mg/kg	117.44±5.60	52.48±8.27	44.80±6.58*
Atropine 5 mg/kg	123.68±3.00	50.26±4.14	44.79±4.24*
ABAQ extract			
Water	103.28±3.87	75.30±1.30	73.36±3.26
100 mg/kg	102.28±2.96	80.80±6.27	78.90±6.71
200 mg/kg	110.00±2.59	86.84±3.82	78.44±2.28
400 mg/kg	108.40±3.03	82.80±2.44	68.19±3.92
Atropine 5 mg/kg	123.68±3.00	50.26±4.14	40.43±2.32*
SBAQ extract			
Water	104.20±4.12	72.20±6.55	74.77±4.77
100 mg/kg	101.60±4.98	76.60±5.03	78.16±1.90
200 mg/kg	110.00±2.59	86.40±3.83	78.44±2.28
400 mg/kg	108.40±3.03	82.80±2.44	76.41±1.25
Atropine 5 mg/kg	108.60±2.01	57.16±4.42	40.43±2.32*
CAQ extract			
Water	104.20±4.12	72.20±6.55	74.77±4.77
100 mg/kg	93.20±2.78	72.20±6.55	78.17±3.91
200 mg/kg	99.80±4.04	77.40±3.36	78.40±5.78
400 mg/kg	96.80±2.82	67.00±2.88	69.71±4.75
Atropine 5 mg/kg	108.60±2.0	57.16±4.42	40.43±2.32*

Values are expressed as mean±SEM (n=5). *P<0.05 significantly different from distilled water treated group. SEM: Standard error of mean; KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

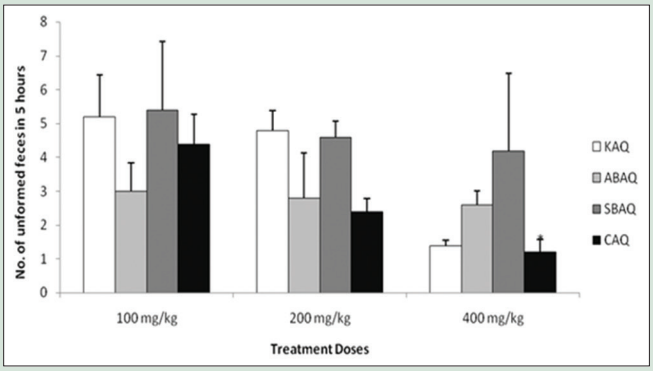

Figure 2: Comparison of inhibition of defecation in rats treated with the different aqueous extracts. KAQ: *Hydnora abyssinica*; ABAQ: *Neorautanenia mitis*; SBAQ: *Vitellaria paradoxa*; CAQ: *Senna surattensis*. *Significantly different from SBAQ in the same cluster

There are no reports of these phytochemicals within the aqueous extract. Alkaloids, tannins, flavonoids, and phenolic phytochemical class types present in these current four plants extracts have been shown to have antidiarrheal activities.[33]

The median lethal dose (LD_{50}) of more than 2000 mg/kg was observed in all the extracts, and the absence of mortality in this study is an indication that the plants are relatively safe. According to OECD, a substance with an LD_{50} >2000 mg/kg is considered relatively safe for experimental purposes.[32]

In the gastrointestinal transit of activated charcoal model, the significant ($P < 0.05$) decrease at all doses of the aqueous extract of *H. abyssinica* when compared to those administered distilled water is an indication of a possible antidiarrheal activity. Diarrhea is defined as the increase in frequency and decrease in consistency of feces. Any substance that can decrease the intestinal motility as seen with the extract of *H. abyssinica* will potentially decrease the rate of stooling. The decrease in motility while increasing the gastric emptying time will cause greater absorption of fluid from the fecal content thereby increasing the consistency of the feces. The decrease was observed to be dose dependent.

When the extracts of the four plants were compared on a dose-to-dose basis, the significant reduction in intestinal motility of rats treated with the extract of *H. abyssinica*, as compared with the extracts from *N. mitis*, *V. paradoxa,* and *S. surattensis,* is an indication of its greater ability to inhibit intestinal motility. This is the first study that compared the effect of these extracts on intestinal motility.

In the castor oil-induced diarrhea study, the dose-dependent inhibition of defecation observed with the *H. abyssinica* extract is a further indication of the antidiarrheal potential of this plant. The significant ($P < 0.05$) dose-dependent reduction in the number of feces excreted by rats treated with extracts of *N. mitis*, *V. paradoxa,* and *S. surattensis* when compared to the control rats treated with distilled water showed that the extracts possess antidiarrheal activity. The antidiarrheal activity of these extracts is mediated in part by a mechanism other than the inhibition of gastrointestinal tract (GIT) motility since the extracts did not inhibit intestinal motility in the transit of activated charcoal meal test.

The inability of the extracts to significantly decrease intestinal motility and ability to significantly inhibit defecation is similar to that observed in albino rats treated with aqueous and ethanol stem bark extracts of *Khaya senegalensis*.[33] The extract of black tea (*Camellia sinensis*), which is used in the management of diarrhea, has also been shown to increase upper gastrointestinal tract motility but decreased intestinal fluid accumulation thereby alleviating diarrhea.[37] Diarrhea can be caused by increased intestinal motility or increased fluid accumulation in the gastrointestinal tract. In the castor oil-induced diarrhea, castor oil when administered orally is broken down to ricinoleic acid. The acid is a gastrointestinal tract irritant that causes inflammation and prostaglandin release.[38] It also alters the permeability of the intestinal mucosa to electrolytes and water hence causing diarrhea.[39]

All of the extracts contained tannins, which may be responsible for the protection against castor oil-induced diarrhea. Tannins are thought to decrease the permeability of the intestinal mucosa to water and electrolytes because of their astringent property.[38]

Table 5: Percentage inhibition of defecation of rats treated with *Hydnora abyssinica* extract, *Neorautanenia mitis* extract, *Vitellaria paradoxa* extract, and *Senna surattensis* extract

Treatment	Mean defecation in 5 h	Percentage inhibition of defecation
KAQ extract		
Castor oil + water	7.8±1.32	-
Castor oil + 100 mg/kg	5.2±1.24	28
Castor oil + 200 mg/kg	4.8±0.58*	38
Castor oil + 400 mg/kg	1.4±0.15*	82
Castor oil + water	0.0±0.00*	100
ABAQ extract		
Castor oil + water	7.8±1.32	-
Castor oil + 100 mg/kg	3.0±0.84*	61
Castor oil + 200 mg/kg	2.8±1.32*	64
Castor oil + 400 mg/kg	2.6±0.40*	66
Castor oil + loperamide 10 mg/kg	0.0±0.00*	100
SBAQ extract		
Castor oil + water	6.2±0.68	-
Castor oil + 100 mg/kg	5.4±2.02	13
Castor oil + 200 mg/kg	4.6±0.46*	26
Castor oil + 400 mg/kg	4.2±2.28*	32
Castor oil + loperamide 10 mg/kg	0.0±0.00*	100
CAQ extract		
Castor oil + water	6.2±0.68	-
Castor oil + 100 mg/kg	4.4±0.86*	29
Castor oil + 200 mg/kg	2.4±0.38*	61
Castor oil + 400 mg/kg	1.2±0.38*	81
Castor oil + loperamide 10 mg/kg	0.0±0.00*	100

Values are expressed as mean±SEM (n=5). *P<0.05 significantly different from distilled water treated group. SEM: Standard error of mean, KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

Table 6: Comparison of inhibition of defecation in rats treated with *Hydnora abyssinica*, *Neorautanenia mitis*, *Vitellaria paradoxa*, and *Senna surattensis* extracts

Treatment (mg/kg)	Percentage inhibition of defecation in rats treated with the extracts			
	KAQ	ABAQ	SBAQ	CAQ
100	28	61	13	29
200	38	64	26	61
400	82	66	32	81

KAQ: Aqueous crude extract of *Hydnora abyssinica*; ABAQ: Crude aqueous extract of *Neorautanenia mitis*; SBAQ: Aqueous crude extracts of *Vitellaria paradoxa*; CAQ: Crude aqueous extract of *Senna surattensis*

CONCLUSION

A preliminary qualitative phytochemical analysis of the aqueous extracts from *H. abyssinica, N. mitis*, *V. paradoxa,* and *S. surattensis* revealed the presence of secondary metabolite classes that have been shown to be

useful in the management of diarrhea. *H. abyssinica* extract appeared to be the most active in the reduction of both intestinal motility and castor oil-induced diarrhea. *N. mitis*, *V. paradoxa*, and *S. surattensis* extracts on the other hand only inhibited defecation in the castor oil-induced diarrhea model. Thus, the studies give credence to the traditional use of these plants to treat the symptoms of diarrhea in humans and livestock. Further studies are necessary to identify the specific phytochemicals in these extracts and to determine their antidiarrheal activities and safety.

Acknowledgement

The management and Staff of the National Veterinary Research Institute Vom are duly recognized for approving the laboratory space for this study. We are indebted to Mr. Yilnya Gosomji, who served as the liaison officer to the Traditional Medical Practitioners and contributed in the collection of plant samples. Mr. Otuwose Agyeno of the Department of Plant Science, University of Jos is acknowledged for assisting with plant identification.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, *et al.* Trends in alternative medicine use in the United States, 1990-1997: Results of a follow-up national survey. JAMA 1998;280:1569-75.
2. Mosihuzzaman M, Choudhary M. Protocols on safety, efficacy, standardization, and documentation of herbal medicine (IUPAC Technical Report). Pure Appl Chem 2008;80:2195-230.
3. McCorkle CM. An introduction to ethnoveterinary research and development. J Ethnobiol 1986;6:129-49.
4. Mathias ME. Magic, myth and medicine. Econ Bot 1994;48:3-7.
5. Rashid MH, Tanzin R, Ghosh KC, Jahan R, Khatun MA, Rahmatullah, M. An ethnoveterinary survey of medicinal plants used to treat cattle diseases in Birishiri area, Netrakona district, Bangladesh. Adv Nat Appl Sci 2010;4:103.
6. Kinman EL. Evaluating health service equity at a primary care clinic in Chilimarca, Bolivia. Soc Sci Med 1999;49:663-78.
7. Nwude N, Ibrahim MA. Plants used in traditional veterinary medical practice in Nigeria. J Vet Pharmacol Ther 1986;3:261-73.
8. Fontaine O. Bacterial diarrhoea and treatment. Lancet 1988;1:1234-5.
9. Audu R, Umilabug SA, Renner JK, Awodiji JA. Diarrhea management. J Niger Infect Control Assoc 2000;3:15-7.
10. Hutton G, Haller L, Bartram J. Global cost-benefit analysis of water supply and sanitation intervention. J Water Health 2007;5:481-502.
11. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, *et al.* Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. Lancet 2012;379:2151-61.
12. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: A review of active surveillance data. Bull World Health Organ 1982;60:605-13.
13. Offiah NV, Makama S, Elisha IL, Makoshi MS, Gotep JG, Dawurung CJ, *et al.* Ethnobotanical survey of medicinal plants used in the treatment of animal diarrhoea in Plateau state, Nigeria. BMC Vet Res 2011;7:36.
14. Luc VP, Norbert DK, Jean-Pierre M, Anthanase G, Niceas S, Jean-Paul D, *et al.* Isolation and structure elucidation of potentially insecticidal and acaricidal isoflovone- type compounds from *Neorautanenia mitis*. J Nat Prod 1987;50:349-56.
15. Sakurai Y, Sakurai N, Taniguchi M, Nakanishi Y, Bastow KF, Wang X, *et al.* Rautandiols A and B, pterocarpans and cytotoxic constituents from *Neorautanenia mitis*. J Nat Prod 2006;69:397-9.
16. Lasisi AA, Adesomoju A. Neoraudiol: A new isoflavonoid and other antimicrobial constituents from the tuberous root of *Neorautanenia mitis* (A.Rich) verdcourt. J Saudi Chem Soc 2015;19:404-9.
17. Vongtau HO, Amos S, Binda L, Kapu SD, Gamaniel KS, Kunle OF, *et al.* Pharmacological effects of the aqueous extract of *Neorautanenia mitis* in rodents. J Ethnopharmacol 2000;72:207-14.
18. Vongtau HO, Abbah J, Mosugu O, Chindo BA, Ngazal IE, Salawu AO, *et al.* Antinociceptive profile of the methanolic extract of *Neorautanenia mitis* root in rats and mice. J Ethnopharmacol 2004;92:317-24.
19. Ndukwe IG, Amupitan JO, Isah Y, Adegoke KS. Phytochemical and antimicrobial screening of the crude extracts from the root, stem bark and leaves of *Vitellaria paradoxa* (GAERTN. F). Afr J Biotechnol 2007;6:1905-9.
20. Lodén M, Andersson AC. Effect of topically applied lipids on surfactant-irritated skin. Br J Dermatol 1996;134:215-20.
21. Nde DB, Boldor D, Astete C, Muley P, Xu Z. Oil extraction from sheanut (*Vitellaria paradoxa* Gaertn C.F.) kernels assisted by microwaves. J Food Sci Technol 2016;53:1424-34.
22. Soladoye MO, Orhiere SS, Ibimode BM. Ethnobotanical study of two indigenous multipurpose plants in the Guinea Savanna of Kwara state – *Vitellaria paradoxa* and *Parkia biglobosa*. In: Biennial Conference of Ecological Society of Nigeria. Ibadan: Forestry Research Institute; 1989. p. 13.
23. El-Mahmood AM, Doughari JH, Ladan N. Antimicrobial screening of stem bark extracts of *Vitellaria paradoxa* against some enteric pathogenic Microorganisms. Afr J Pharm Pharmacol 2008;2:89-94.
24. Eyong KO, Foyet HS, Baïrys G, Ngosong Folefoc G, Acha Asongalem E, Lagojda A, *et al.* A new ursane triterpenoic acid and other potential anti-inflammatory and anti-arthritic constituents from EtOAc extracts of *Vitellaria paradoxa* stem bark. J Ethnopharmacol 2015;174:277-86.
25. Usha V, Bopaiah AK. Phytochemical investigation of the ethanol, methanol and ethyl acetate leaf extracts of six *Cassia* species. Int R J Pharm Sci 2012;3:34-9.
26. Musselman LJ, Visser JH. Taxonomy and natural history of *Hydnora* (Hydnoraceae). Aliso 1989;12:317-26.
27. Yagi S, Chrétien F, Duval RE, Fontanay S, Maldini M, Piacente S, *et al.* Antibacterial activity, cytotoxicity and chemical constituents of *Hydnora johannis* roots. South Afr J Bot 2012;78:228-34.
28. Wintola OA, Afolayan AJ. The antibacterial, phytochemicals and antioxidants evaluation of the root extracts of *Hydnora africana* Thunb. used as antidysenteric in Eastern Cape province, South Africa. BMC Complement Altern Med 2015;15:307.
29. Dawurung CJ, Elisha IL, Offiah NV, Gotep JG, Oladipo OO, Makoshi MS, *et al.* Antidiarrheal evaluation of aqueous and ethanolic leaf extracts of *Acacia sieberiana* DC. (Fabaceae) in albino rats. Asian J Exp Biol Sci 2012;3:799-803.
30. Prapalert W, Santiarworn D, Liawruangrath S, Liawruangrath B, Pyne SG. Two phenyllethanoid glycosides, parvifloroside A and B, isolated from *Barleria strigose*. Chiang Mai J Sci 2016;43:18.
31. Sasidharan S, Chen Y, Sundram KM, Yoga Latha L. Extraction, isolation and characterization of bioactive compounds from plants'extracts. Afr J Tradit Complement Altern Med 2011;8:1-10.
32. Organisation for Economic Cooperation and Development. Acute Oral Toxicity-Fixed Dose Procedure. OECD Guidelines for the Testing of Chemicals, 420. Paris: Organisation for Economic Cooperation and Development; 2001.
33. Elisha IL, Makoshi MS, Makama S, Dawurung CJ, Offiah NV, Gotep JG, *et al.* Antidiarrheal evaluation of aqueous and ethanolic stem bark extracts of *Khaya senegalensis* A. Juss (*Meliaceae*) in albino rats. Pak Vet J 2013;33:32-6.
34. Chitme HR, Chandra M, Kaushik S. Studies on anti-diarrhoeal activity of *Calotropis gigantea* R.Br. in experimental animals. J Pharm Pharm Sci 2004;7:70-5.
35. Saadabi AM, Ayoub SM. Comparative bioactivity of *Hydnora abyssinica* A. Braun against different groups of fungi and bacteria. J Med Plants Res 2009;3:262-5.
36. Kabila B, Sidhu MC, Ahluwalia AS. Phytochemical profiling of different *Cassia* species: A review. Int J Pharm Biol Arch 2017;8:12-20.
37. Besrea SE, Ganguly DK, Vedasiromoni JR. Antidiarrheal activity of hot water extract of Black Tea (*Camellia sinensis*). Phyther Res 2003;17:380-4.
38. Chaulya NC, Halder PK, Mukherjee A. Antidiarrheal activity of methanol extract of rhizomes of *Cyperus tegetum* Roxb. Int J Pharm Pharm Sci 2011;3:133-5.
39. Kumar B, Divakar K, Tiwari P, Salhan M, Goli D. Evaluation of antidiarrheal effect of aqueous and ethanolic extracts of fruit pulp of *Terminalia belerica* in rats. Int J Drug Dev Res 2010;2:769-79.