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Scientific investigation and standardization of commercially available herbal formulations for the control of diarrhea and gastrointestinal motility

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Abstract

Context: Akseer-e-Pachish and Pachrin syrup are the two branded herbal medicines marketed widely for their antidiarrheal property. Objectives: This study is focused to investigate the antidiarrheal effect of both products and to provide scientific background for their activity. Material and Methods: Both herbal brands were evaluated against different types of diarrhea induced by castor oil (1 ml/kg), magnesium sulphate (2 mg/kg) and clarithromycin (100 mg/kg) using pigeon model. Charcoal activity was used for determination of changes in GI transit time. Results: Both brands confirmed significant ($p<0.001$) reduction in average weight of stool. Discussion and conclusion: Significant ($p<0.01$) decrease in intestinal motility was also noticed for both brands. Conclusion: It was concluded that both herbal medicines have anti-diarrheal effect on the basis of findings.

Key Words: Akseer-e-Pachish, Pachrin, Loperamide, Anti-diarrheal, Charcoal test, Acute toxicity Test.

Introduction

The condition in which a person have at least three times loose or liquid bowel movement per day is known as Diarrhea and main cause is Rotavirus among children throughout the world (1). Diarrhea involves an increase in the gastrointestinal motility with enhancement of secretion as well as reduction of absorption of fluid, resulting loss of electrolytes specially sodium ions and water (2). Notwithstanding, multiple therapies are existing in allopathy and homeopathy but we are still required cheap, efficient, everywhere and easily available treatment. Allopathic standard drug is Loperamide in high dose but it's rate of failure is significant (3). In addition, WHO and American Academy of Pediatrics persuade health care professionals, not to use loperamide in children for safety reason (4), wheras Diarrhea killed 0.751 million out of 7.6 million children, younger than 5 years in 2010 (5). The dependency of majority people on herbal medicines especially in developing countries is about 80% and its sale is increasing day by day (6). So, we have chosen two dissimilar branded herbal formulations, Akseer-e-Pachish (AK) by Qarshi Industries (pvt) Ltd and Pachrin syrup (Pach) by Mumtaz Dawakhana available for validation of their claimed anti-diarrheal effect because these are available in market without any scientific background.

Materials and Methods

Chemicals and drugs

We purchased Loperamide HCl (Bryon Pharmaceutical), Castor oil (Abbott Laboratories), Clarithromycin (Getz Pharmaceutical), and Metronidazole (Stanley Pharmaceuticals) from local market.

Formulation AK (Akseer-e-Pachish by Qarshi Industries pvt Ltd)

Common name	Botanical Name	Part used
Pomegranate	Punica granatum	Fruit
Babul	Acacia Nitolica	Bark
Fennel	Foeniculum Vulgare	Seed
Myrtle	Myrtus Communis	Seed
Fennel	Foeniculum Vulgare	Oil
Sodium Benzoate	--	Preservative

Formulation Pach (Pachrin Syrup by Mumtaz Dawakhana)

Common name	Botanical Name	Part used
Carom	Trachyspermum Ammi	--
Pomegranate	Punica granatum	Flower
Sweet Barley	Hordeum Vulgare	--
Mochrus	Bombax Malabaricum	--
Plantain	Musa Paradisiaca	--
Dried Mint	Mentha Spicata	--
Myrtle	Myrtus Communis	--
Pomegranate	Punica granatum	Seeds
Anise	Pimpinella Anisum	--
Chinese Cassia	Cinnamomum Cassia	--
Phyllantus	Phyllantus Maderaspatensis	Seeds
Tamarix	Tamarix Articulata	--
Bistort	Polygonum Viviparum	--
Acacia	Acacia Arabica	--
Cabonate Rock	--	--

Experimental Animals

We bought healthy pigeons of both sexes from local market and brought to the laboratory of Pharmacy Department, Abdul Wali Khan University Mardan, Pakistan. The control environment was available to pigeons for 1 week. After observation, we selected animals having good health. The temperature (25 ± 2°C), humidity (55-65%) and 12-hour light/dark cycle was provided. Further, protocols of study were approved by Ethical committee of university and we removed animals having problems in movement, drinking and eating.

Grouping and Dosing

We randomly divided specific pigeons into four groups and each group had six pigeons. Distilled water was selected as negative control and loperamide as positive control whereas remaining were test groups.

Acute toxicity test

We executed acute toxicity test for both brands in single and multiple doses (7) and gave 2.5, 5 and 10 ml/kg doses of test samples to pigeons. We observed every movement alteration as well as change in eating and drinking for 4 h, while animals were kept under observation for 24 h for possible lethal effect.

Induction of Diarrhea

We induced diarrhea by magnesium sulphate (2gm/kg), castor oil (1 ml/kg) and clarithromycin (100 mg/2ml) in pigeons, already administered with distilled water (10 ml/kg), loperamide (1 ml/kg) and both products at 0.5, 1, and 1.5 ml/kg doses. We kept animals in separate cages with covered base by pre-weighed white paper. We determined number of defecation, time for first drop, second drop and weight of stool as per standard protocols (8). Percent inhibitory effect on diarrhea of each sample was calculated using the following relationship.

$$\%\ \text{inibition} = \frac{\text{stool weight of control} - \text{stool weight of test group}}{\text{stool weight of control}} \times 100$$

Gastrointestinal motility test

We divided all pigeons into five groups and kept on fasting for 24 h with free access to water. Group 1 and 2 was administered with distilled water and castor oil where Group 3 received 1 ml metronidazole whereas Group 4 and 5 served were given branded herbal formulations at different doses. Charcoal was provided to all pigeons after 5 minutes and animals were given free access to drinking water for 30 minute. After that, Pigeons were sacrificed and intestine was removed for the calculation of percent motility using following method (9).

$$\%\ \text{Motality} = \frac{\text{Distance travelled by drug}}{\text{Total length of small intestine}} \times 100$$

Statistical analysis

All experiments were carried out in triplicate. Statistical analysis was finalized by one-way analysis of variation (ANOVA) followed by Dunnett's tests, p values <0.05 were considered statistically significant.

Results

Acute Toxicity Test

Observations of acute toxicity test are given in Table 1. Both formulations showed nausea and vomiting at higher dose where deaths were recorded with a dose of 10 ml/kg only.

Table 1: Acute toxicity of selected formulations

Gp	Dose (ml/kg)	Jerk	Vomiting	Deaths
DW	10	--	--	--
AK	2.5	Yes	Yes	--
	5	Yes	Yes	--
	10	--	Severe	4
Pach	2.5	Yes	--	--
	5	--	Yes	--
	10	--	Severe	3

DW (Distilled Water), AK (Akseer-e-Pachish), Pach (Pachrin), n = 6

Effect of selected herbal formulation on Magnesium sulphate induced diarrheal Model Ak and Pach displayed dose-dependent anti-diarrheal effect against magnesium sulphate induced diarrhea. Both brands significantly ($p < 0.05$) reduce total no. of defecations at 1.5 ml/kg dose. Both products significantly ($p < 0.05$) reduced diarrheal feces at 0.5 ml/kg while all other doses of both tested products significantly ($p < 0.01$) decreased diarrheal feces. Both brands significantly ($p < 0.001$) reduced average weight of stool at all doses. Ak inhibited 11.01, 19.43 and 27.43 % and Pach has 9.66, 15.55, and 21.63 % average stool at 0.5, 1, and 1.5 ml/kg respectively.

Table 02. Effect pf selected herbal formulations on Magnesium Sulphate induced diarrhea

Gp	Dose (ml/kg)	No. of Defecation	Diarrheal Feces	Average weight (mg)	%Inhibition
DW	10	16.35±1.55	12.45±1.78	3563.75±2.5	-
Ak	0.5	10.24±1.73	4.11±1.23*	3171.15±3.12***	11.01
	1.0	08.45±1.15	2.31±1.25**	2870.98±3.21***	19.43
	1.5	07.20±1.15*	3.26±3.07**	2585.87±3.23***	27.43
Pach	0.5	10.99±1.20	4.43±4.32*	3219.30±2.14***	9.66
	1.0	09.11±1.73	3.18±2.30**	3009.32±5.01***	15.55
	1.5	08.43±1.44*	2.09±1.31**	2792.90±5.11***	21.63
Lop	1	6.33±1.44*	1.12±2.14**	1903.21±3.69***	46.59

Data are presented as mean ± standard error of the mean for groups (n = 6), one-way ANOVA followed by Dunett's test was applied for data analysis* ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$) versus negative group

Effect of selected herbal formulation on Castor Oil induced diarrhea

Both branded herbal formulations showed insignificant anti-diarrheal effect against castor oil induced diarrhea. Total no. of defecations was insignificantly decreased by both tested products. Ak significantly ($p < 0.05$) reduced diarrheal feces at dose of 0.5 ml/kg and rest of doses of both brands were insignificant for reduction of diarrhea. Average weight was significantly ($p < 0.001$) decreased by both brands at every dose. Ak has 12.84, 20.02 and 24.10 % inhibition whereas Pach has 10.67, 18.59 and 21.16 % inhibition at 0.5, 1, and 1.5 ml/kg respectively.

Table 03. Effect of selected formulations on Castor oil induced diarrheal Model

Gp	Dose (ml/kg)	No. of Defecation	Diarrheal Feces	Average Weight (mg)	% Inhibition
DW	10	16.35±1.55	12.45±1.78	3563.75±2.5	-
Ak	0.5	11.06±0.80	3.16±1.19*	3106.07±4.12***	12.84
	1.0	9.53±1.03	3.52±4.17	2850.15±3.13***	20.02
	1.5	8.03±1.09	3.21±4.25	2704.85±5.01***	24.10
Pach	0.5	11.95±0.75	5.07±3.63	3183.49±3.63***	10.67
	1.0	10.12±1.09	4.43±3.36	2901.03±2.88***	18.59
	1.5	9.46±1.10	4.09±1.32	2809.63±4.26***	21.16
Lop	1	5.71±0.72	2.44±4.63*	1851.37±3.13***	46.59

Data are presented as mean ± standard error of the mean for groups (n = 6), one-way ANOVA followed by Dunett's test was applied for data analysis* ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$) versus negative group

Effect of selected herbal formulation on Clarithromycin induced diarrhea

Ak and Pach expressed significant anti-diarrheal effect against castor oil induced diarrhea. Both tested products significantly decreased total no. of defecations at 1.5 ml/kg dose while other doses of both brands were insignificant to reduce total no. of defecations. Ak significantly ($p < 0.01$) reduced diarrheal feces at 0.5 and 1.5 ml/kg while at 1 ml/kg dose, both products significantly ($p < 0.05$) diarrheal feces and Pach not significantly reduced diarrheal feces at 0.5 and 1.5 ml/kg dose. Average weight was significantly ($p < 0.001$) reduced by both herbal formulations at 0.5 and 1 ml/kg whereas both brands significantly ($p < 0.01$) decreased average weight at dose of 1.5 ml/kg. Ak inhibited 13.3, 20.38, 26.95 % and RKS 12.75, 18.43 and 23.66 % at 0.5, 1, and 1.5 ml dose, respectively.

Table 4: Effect of selected formulations on clarithromycin induced diarrheal model

Gp	Dose (ml/kg)	No. of Defecation	Diarrheal Feces	Average Weight (mg)	% Inhibition
DW	10	16.35±1.55	12.45±1.78	3563.75±2.5	-
Ak	0.5	11.56±1.06	2.11±5.04**	3088.50±2.32***	13.33
	1.0	09.43±3.86	2.01±2.43*	2837.43±3.63***	20.38
	1.5	7.21±0.92*	2.53±2.24**	2603.21±4.23*	26.95
Pach	0.5	12.23±0.98	4.14±3.42	3109.17±2.72***	12.75
	1.0	10.21±5.9	2.42±3.24*	2906.91±4.35***	18.43
	1.5	07.92±1.06*	3.91±3.36	2720.40±3.50*	23.66
Lop	1	6.33±1.44*	1.12±2.14**	1903.21±3.69***	46.59

Data are presented as mean ± standard error of the mean for groups (n = 6), one-way ANOVA followed by Dunett's test was applied for data analysis* ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$) versus negative group

Gastrointestinal Motility Test

Both the products decreased the normal intestinal movements of charcoal meal in a dose dependent way. Ak has 42.29, 39.93, and 35.12 percent motility while Pach has 44.77, 41.17, and 38.09 percent motility at 0.5, 1, and 1.5 ml/kg dose.

Table 5: Effect of selected formulations on GIT motility in pigeon model

Gp	Dose (ml/kg)	Distance travelled	Total distance	% motility
DW	10	26.08±3.09	43.13±4.23	60.44±3.09
Castor oil	01	22.69±3.42**	39.63±2.09	57.25±2.98
Metronidazole	01	8.52±4.38*	41.53±2.90	19.86±1.75
Ak	0.5	17.65±1.39	41.73±2.88	42.29±2.75*
	1	17.30±2.98	43.32±2.23	39.93±0.72**
	1.5	14.52±1.32	41.34±4.35	35.12±0.75 ***
Pach	0.5	18.32±3.08	40.92±2.38	44.77±1.86*
	1	17.94±2.53	43.57±2.93	41.17±0.77**
	1.5	16.20±4.01	42.52±2.19	38.09±0.86 **

Data are presented as mean ± standard error of the mean for groups, * ($p < 0.05$), ** ($p < 0.01$) (n = 6)

Discussion and Conclusion

Magnesium sulphate inhibits reabsorption of water ions which enhances intestinal content volume and encourages release of cholecystokinin from duodenal mucosa which is responsible for increase motility as well as secretion of small intestine. So, it stops absorption of sodium chloride and water (10). Both branded products displayed a non-significant effect against magnesium sulphate induced diarrhea. so, it may be expected that osmotic properties of the GIT may not be involved in this study. Castor oil induces diarrhea due to formation of ricinoleic acid. Ricinoleic acid is it's active and is produced by process of hydrolysis in the upper small intestine. It releases prostaglandin by irritation and inflammation of the intestinal mucosa which alters water secretion and electrolyte transport, resulting in a hyper-secretory response in the small intestine (11, 12). We removed anti-secretory mechanism of both brands because of non-significant anti-diarrheal effect. Clarithromycin alters normal colonic micro-flora and produces diarrhea (13). Both branded herbal formulations contain herbs having anti-diarrheal and anti-bacterial activity. So, it's observed anti-diarrheal response may be related to their composition and reduced diarrhea through different mechanism of action. These herbal products effectively treat diarrhea initiated by antibiotics.

This experimental work has proven claimed anti-diarrheal effect of both branded herbal formulations and their activity is proportional to their composition. We strongly recommend these herbal medicines for their specific anti-diarrheal response because of scientific background, local availability, and low price but government should check their standard for benefit of people.

References

1. Umesh D. Parashar, Christopher J. Gibson, Joseph S. Bresee, Roger I. Glass.: Rotavirus and severe diarrhea, Emerging Infectious Diseases 2006; 304-306.
2. Chisti M.J., Pietroni M.A., Smith J.H., Bardhan P.K., Salam M.A.: Prevalence, Clinical Predictors, and Outcome of Hypocalcaemia in Severely-malnourished Under-five Children Admitted to an Urban Hospital in Bangladesh: A Case-Control Study Journal of Health, population and Nutrition 2014; 270-275.
3. Vassilious Barbounis, George Koumakis, Micheal Vassilomanolakis, Matina Demiri, Anna P. Efremidis.: Control of irinotecan-induced diarrhea by octreotide after loperamide failure.: Supportive Care in Cancer 2001; 258.
4. Unger-Chan C., Sharmin-Salam S., Sarker-Alam S., Black R., Cravioto A., Arfeen-El S.: Treating diarrheal disease in children under five: the global picture.: Archives of Diseases in Childhood, British Medical Journal.: 2014; 99.
5. Li Liu PhD, Hope L Johnson PhD, Prof Simon Cousens MA, Jamie Perin PhD, Susana Scott PhD, Joy E Lawn PhD, Prof Igor Rudan MD, Prof Harry Campbell MD, Richard Cibulskis PhD, Mengying Li MSPH, Colin Mathers PhD, Prof Robert E Black MD.: Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2010.: The Lancet.: 2012; 2151.
6. Gail B. Mahady.: Global harmonization of herbal health claims.: The American Society of Herbal Health Claims.: 2001; 162.
7. S Meite, J D N'guessan, C Bahi, H F Yapi, A J Djaman, F Guede Guina.: Antidiarrheal activity of the ethyl acetate extract of morinda morindoides in rats.: Tropical Journal of Pharmaceutical Research.: 2009; 201.

8. E. Y. Qnais, A.S. Elokda, Y. Y. Abu Ghalyun, F. A. Abdulla.: Antidiarrheal activity of the aqueous extract of punica granatum.: Pharmaceutical Biology.: 2008; 715.
9. Ihsanullah, Fazal Subhan, Khalid Rauf, Amir Bangash, Gowhar Ali.: Role of gastrointestinal motility/gastric emptying in cisplastin-induced vomiting in pigeons.: African Journal of Pharmacy and Pharmacology.: 2012; 2592.
10. Rozina Rouf, Shaikh Jamal Uddin, Jamal Ahmad Shilpi, Mahiuddin Alamgir.: Assessment of antidiarrheal activity of the methanol extract of Xylocarpus granatum bark in mice model.: Elsevier.: 2007; 539.
11. T S Gaginella, J J Stewart, W A Olsen and P Bass.: Actions of Ricinoleic acid and structurally related fatty acids on the gastrointestinal tract. II. Effects of water and electrolyte absorption in vitro.: The Journal of Pharmacology and Experimental Therapeutics.: 1975. 355.
12. Rao N.V., Prakash K.C., Kumar S.M.S.: Pharmacological Investigation of Cardiospermum Halicacabum (Linn).: Indian Journal of Pharmacology.: 2006; 346.
13. Rafii R., Sutherland J.B., Cerniglia C.E.: Effects of treatment with antimicrobial agents on the human colonic microflora.: Therapeutics and clinical risk management 2008; 1343.