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In Vivo Study on Laxative Effect of *Prunus amygdalus* Oil

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ABSTRACT

Objective: *In this study, we assessed the laxative effects of Prunus amygdalus oil (PAO) in constipation model of mice.* ***Method:*** *The animals were divided into 6 groups and Prunus amygdalus oil was orally administered in two dose-strengths (3.0 ml/kg/day and 6.0 ml/kg/day) in mice. Group one was administered with Lactulose (30 ml/kg/day) as standard. Understandings of the possible mechanism of laxative action 2 groups of animals were pretreated with atropine (10 ml/kg/day) that moderately inhibit the laxative activity of Prunus amygdalus oil.* ***Results:*** *Results of our study revealed that treatment of PAO was effective in increasing the fecal number and fecal weight and this increase was very close to standard drug Lactulose, which indicate the laxative activity of oil. Those groups of animals which were previously administered with atropine partially inhibit the laxative activity of Prunus amygdalus oil, specifying that laxative action is mainly facilitated through muscarinic receptors activation and indicated the occurrence of Acetylcholine like component.* ***Conclusion:*** *Our study results revealed the laxative activity of PAO mediated mainly with the cholinergic pathway. This study provides a basis for beneficial use of Prunus amygdalus oil in constipation.*

Keywords: *Prunus amygdalus* oil, Laxative effect, Constipation

INTRODUCTION

A systematic review reported constipation in 0.7% to 29.6% in pediatric children. The functional constipation occurrence in children is 4% to 36% [1,2]. Particular mechanism of developing functional constipation is not clear in children but there are a majority of cases as functional constipation. The frequency of evacuation is greatly affected by child age. In the neonatal age group, evacuation may occur 4-6 times a day and gradually decreases to 1-2 per day, till the period of early age ends it may be 4 years. In infants, younger than 4 months, the type of feeding has an important role in the evacuation pattern. Healthy infant breast-fed babies may defecate in routine 7 times per day or uncommonly one time per week [3,4]. Literature shows bowel movement in neonates and 3 months older 2.0 to 2.9 per day and infants more than 3 month and kids up to 3 years have 1.8 and 1.4 evacuations per day [3-5]. The etiology of functional constipation depends on both functional constipation that includes developmental disorder (ADHD and autism) and occasional constipation includes (toilet training, phobia, and aggressive parental behavior), psychological (depression) and several other factors also contribute like genetic, environmental and dietary [6,7].

Prunus amygdalus Oil

Prunus amygdalus (commonly known as almond, badaam) belongs to the family Rosaceae, scientific name *Prunus amygdalus* and globally number one nut producing tree [8]. *Prunus amygdalus* oil (PAO) has been used as a medication for its several health benefits and also in cosmetics. The main constituents of the oil are triacylglycerides, free fatty acids, diacylglycerides, mono-acyl glycerides and sterols present in a minor amount. PAO is abundant in beta-zoosterol, squalene and alpha-tocopherol that is worthy for skin and majorly contain essential fatty acids, carbohydrate and protein and also very important vitamins and minerals specifically vitamin B complex and zinc [9]. *Prunus amygdalus* have been used pharmacologically for irritable bowel syndrome and colonic cancer, cardiovascular and cholesterol lowering action, lipid lowering action, hemorrhoids, hypoglycemic action, hepatoprotective action,

immuno-stimulant action, amnesia action, pre-biotic potential, antioxidant, antistress and prominent laxative action [10-21]. PAO is also being successfully used in aroma therapy, cosmetic purpose and as a staple diet [9,10].

Standard Drug Lactulose

Lactulose is suggested as an effective and well accepted management of constipation in kids [22]. Lactulose is synthetic disaccharide among the osmotic agents unabsorbed through the small intestine and easily digested through colonic bacteria [23]. Lactulose breakdown into lactic acid and acetic acid, acidify the intestinal substance that retains hydration of feces by osmosis that makes them easy to pass. Lactulose intracolonic fermentation can concomitant the making of gases with colic bloating and flatulence. Long term use of lactulose can cause variations in the colonic bacterial breakdown and a decrease in the efficacy of the management of prolonged constipation [24].

MATERIALS AND METHODS

Plant Oil

The *Prunus amygdalus* oil was obtained from S. Ather and Brothers Karachi Sindh Pakistan.

Animals

In the controlled environment (25 ± 2°C) and relative humidity (30% to 70%) animal house of the Ziauddin University kept local breed BALB/c weighing (20-30 g). The animals were set in separate standard cages and routine they had fed with standard diet and water ad libitum while during testing they fasted. The study protocols were approved by the Board of Advance Studies and Research Ziauddin University and were conducted with the "Guidelines for care and use of laboratory animal 8th edition" [25]. Prior approval from the Ethics Review Committee (ERC) of Ziauddin University was obtained before conducting this study.

Laxative Activity Test

Fasted for 6 h BALB/c mice of either sex located separately in animal cages lined with fresh filter paper before testing of drugs. Mice were alienated into 6 groups, each containing (n-6) mice. Every group was treated as follows:

- Group-1 (G-1) was treated with 10% DMSO and 5% Tween-80 in distilled water (10 ml/kg/day, p.o), which was marked as a negative control [26]
- Group-2 (G-2) was administered with Lactulose (30 mg/kg/day, p.o) and marked as a positive control [27]
- Group-3 (G-3) was treated with PAO (3.0 ml/kg/day, orally, p.o) [28]
- Group-4 (G-4) was treated with PAO (6.0 ml/kg/day, orally, p.o) [28]
- To understand the possible mechanism of laxative effect, 2 groups of mice (Groups 5 and 6) had been administered atropine (10 mg/kg, i.p.) one hour earlier the administration of PAO [26]. After 24 h, all feces (dry and wet) in all mice were collected and counted, and rise in wet feces consider as laxative effect [29,30].

Acute Toxicity Studies

An acute toxicity study was performed in 4 groups of mice (n=6). We administered increased doses of PAO (100 ml/kg/day and 200 ml/kg/day, p.o.) into 2 groups (Group T1 and Group T2). Third group (Group T3) of mice was treated with 10% DMSO and 5% Tween-80 in distilled water (10 ml/kg/day, p.o), which was marked as a negative control and fourth group (Group T4) of mice treated with Lactulose (300 mg/kg/day, p. o) and was marked as positive control. The animals were fed with standard diet and water ad libitum kept under monitoring for 6 h to monitor their behavioral changes, piloerection, blindness, whereas lethality was observed up to 24 h [26].

RESULTS

Laxative Effect of *Prunus amygdalus* Oil (PAO)

PAO treatment produced an increase in wet feces. Oral administration of PAO at doses of 3.0 ml/kg/day and 6.0 ml/kg/day and the percent increase in wet feces was 40.55 ± 0.15 and 66.04 ± 1.04 respectively, which is near to the normal positive control value 68 ± 0.24% in the lactulose treated group. One hour prior administration of atropine (10 mg/kg; i.p.), partly inhibit the laxative activity of PAO with resultant values of 16.7 ± 0.17% and 30.44 ± 0.28% at the

separate doses of 3.0 ml/kg/day and 6.0 ml/kg/day in mice. The detailed outcomes of laxative activity are presented in Table 1.

Table 1 Laxative activity of *Prunus amygdalus* oil

Group No.	Treatment	Dose Administered (ml/kg/day)	Route of Administration	Mean of Total No. of Feces	Mean of Total No. of Wet Feces	Laxative Effect (%)
G-1	10% DMSO and 5% Tween-80 in DW	10	p.o	3.28 ± 0.27	0	0
G-2	Lactulose	30	p.o	19.09 ± 1.07	13 ± 0.23	68 ± 0.24
G-3	*Prunus amygdalus* oil	3.0	p.o	10.11 ± 0.38	4.1 ± 0.11	40.55 ± 0.15
G-4	*Prunus amygdalus* oil	6.0	p.o	18.29 ± 1.10	12.08 ± 0.34	66.04 ± 1.04
G-5	Atropine+*Prunus amygdalus* oil	10+3.0	i.p, p.o	7.78 ± 0.31	1.3 ± 0.15	16.7 ± 0.17
G-6	Atropine+*Prunus amygdalus* Oil	10+6.0	i.p, p.o	15.11 ± 1.04	4.6 ± 0.06	30.44 ± 0.28
Results are presented as mean ± S.E.M. n-6. $p<0.05$. The p.o Symbolize oral, while i.p Symbolize intraperitoneal						

Acute Toxicity Studies

Acute toxicity studies resulted in safe dose administration. The results revealed both groups of mice (Group T1 and T2), treated with PAO (100 ml/kg/day and 200 ml/kg/day, p.o. respectively) demonstrated usual behavior and active status.

DISCUSSION

Prunus amygdalus has been used traditionally for the management of many disorders and also in constipation although no clinical data is available for the laxative activity of *Prunus amygdalus* oil (PAO) [31]. Constipation is wide spread functional gastric disorder, disturbing the quality of life in constipated persons [32]. In this study, we assessed the laxative effects of PAO in mice. The treatment with PAO was effective and increased the fecal number and fecal weight, which shows the laxative activity of the oil. To understand the mechanism involved in the laxative activity PAO, animals were prior treated with atropine, which partly inhibits the laxative activity of the oil, specifying that laxative action is mainly facilitated through muscarinic receptors involvement [33], indicating the occurrence of Acetylcholine (ACh) like component. The main excitatory neurotransmitter of the enteric nervous system is acetylcholine [34]. ACh activates muscarinic receptors provide a base for gastric stimulation. The existenceof ACh-like action may increase its usage in medicine.

CONCLUSION

Our study results revealed that PAO exhibit the laxative activity mediated primarily with the cholinergic pathway. This study provides a rationale for the therapeutic use of *Prunus amygdalus* oil in constipation.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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