Journal of Aging Research & Clinical Practice©
Volume 2, Number 1, 2013

PHARMACOLOGICAL, BIOCHEMICAL AND TOXICOLOGICAL EVALUATION OF POTASH ALUM AS ANTI-OBESITY AGENT

Z. Ahmed[1], I. Kazmi[1], M. Afzal[1], M. Pravez[2], R. Singh[1], S. Saleem[3], R. Kaur[1], F. Anwar[1]

Abstract: The objective of present study was to evaluate the role of Potash Alum as an anti obesity agent in Wistar rats fed on high fat diet (HFD). Animals were fed on HFD (58% fat) with or without Potash Alum for 24 weeks. Results revealed that oral intake of Potash Alum exhibited significant reduction in body weight, food intake, serum triglycerides (TG), total cholesterol (TC), high density lipoproteins (HDL), alkaline phosphatase (ALP), serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT) whereas simultaneously increased the dry weight of feces, total lipids in feces, in kidneys and liver compared to HFD fed control. Furthermore, a particularly new observation i.e., the enlargement of teeth along with gummosis was noticed with the treatment.

Key words: Obesity, potash alum.

Introduction

The current approach of treatment for obesity includes behavioral therapy aimed at modifying eating related activities (1); Most of the medicinal therapy is of organic composition. Life on the earth is carbon based due to its properties of forming bond with itself and other atoms. Lesser work has been done on the inorganic salts by the researchers in the modern medical therapy. Therapeutic efficacy of inorganic salt aluminum and its compound has been evaluated in many diseases (2, 3). Of which Potash Alum has been used in the treatment of neoplasm in vivo without causing its side effects and thus increasing the life expectancy (4).

On the basis of existing literatures and research works, the present study is aimed for pharmacological evaluation of the Potash Alums on the high fat fed induced obesity.

1. Siddhartha Institute of Pharmacy, Dehra Dun, Uttarakhand, India; 2. Jamia Hamdard, New Delhi, India; 3. Department of Pharmacology, Luqman College of Pharmacy, Gulbarga, Karnataka

Corresponding Author: Dr. Muhammad Afzal, Assistant Professor, Siddhartha Institute of Pharmacy, Dobachi, Near IT Park, Dehradun-248001, Uttarakhand, India, Tel.: +91 7579241651, E-mail: afzalgufran@gmail.com

Co-corresponding Author: Dr. Firoz Anwar, Prof. and Dean (Research & Academic), Siddhartha Institute of Pharmacy, Dobachi, Near IT Park, Dehradun-248001, Uttarakhand, India, Tel.: +91 9412937329, E-mail: firoz_anwar2000@yahoo.com

Received January 2, 2012
Accepted for publication September 13, 2012

Materials and Methods

Animals

Healthy male Wistar rats weighing 100-150g were procured from central animal house facility of Siddhartha Institute of Pharmacy, Dehradun, India. The animals were divided into 6 groups (n=6). Group I (normal control rats) received normal diet daily for 24 weeks. Group II (disease control rats) received HFD during whole study. Group III (prophylactic group) received Potash Alum + HFD during whole experiment, Group IV (therapeutic group) received HFD + Potash Alum during experiment, Group V received HFD for 15 days then kept on normal diet and administered Potash Alum during the study and Group VI (Alum control) received Potash Alum with normal diet during whole experiment.

Rats were fed with HFD for 2 weeks prior to Potash alum treatment. Potash Alum was administered orally twice daily in the dose of 9.0 mg/kg of body weight.

Estimation of biochemical parameters and lipid content of feces

Blood samples were collected on termination of the experiment from retro orbital plexus; were allowed to stand for 30 minutes at room temperature and centrifuged at 2500 rpm for 10 minutes to separate the serum and TC, TG, HDL, SGOT, SGPT, ALP, albumin

and total bilirubin were determined using Standard kit with semi-auto analyzer (Photometer 5010, Nicholas India Pvt. Ltd).

Fecal lipids (collected in last 3 days of the experimental period) were determined gravimetrically by a modification of the Saxon method.

Histopathological Analysis

The kidneys were preserved in phosphate buffered 10% formalin, embedded in paraffin and used for histopathological examination.

Statistical Analysis

Data are expressed as Mean ± S.E.M. Where n=6. ap<0.05; bp<0.01; cp<0.001 compared to HFD fed control (one way ANOVA followed by Tukey's post-test).

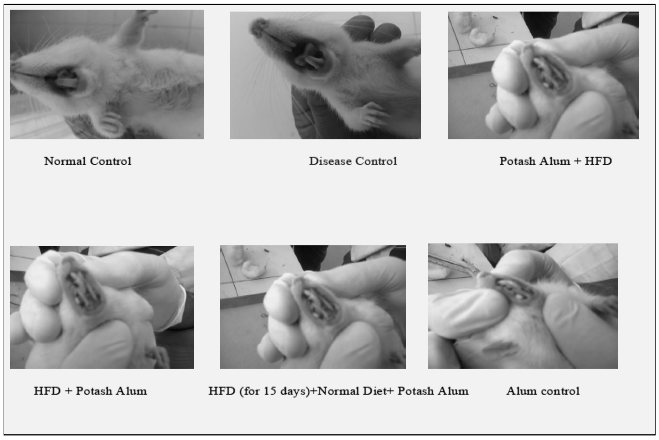
Toxicity study

A new and remarkably significant (P<0.01 and 0.001) toxicity was observed in different groups treated with Potash Alum. It was found that there was an enlargement of teeth as compared to normal and disease control groups. Furthermore, there was marked decrease in body weights, increase in lethargicity along with pungent smell in the fecal content with constipation. Tumor like growths in the lower jaw of the alum control animals was also observed (Fig. 1).

Result and Discussion

In the present study. It was found that the consumption of HFD by rats for 24 weeks increased the body weight might be due to the consumption of an energy rich diet of saturated fats and its deposition in body pads coupled with decreased energy expenditure when compared to NPD fed rats (Normal control). Treatment with Potash Alum to HFD fed rats reduced the increase in body weight (Table 1).

Figure 1
Photographs of rats teeth showing teeth sizes in different groups (a). Normal (b). Normal (c). Increased (d). Increased (e). Increased (f). Increased



There was an increase in fecal weight and TG the treated group (Alum + Obese group) compared to HFD fed rats (Disease control). From this observation it can be hypothesized that Potash Alum might have inhibited pancreatic lipase or bind TG to increase fecal excretion.

The hypertriglyceridemia observed in HFD fed rats may be due to increased absorption and formation of triglycerides in the form of chylomicrons from exogenous fat-rich diet or through combination of increased endogenous production of TG enriched hepatic VLDL and decreased TG uptake in peripheral tissues (5).

We observed increased level of liver TG and serum lipids such as STG, STC, LDL and VLDL in HFD fed rats. Furthermore, hyperlipidemia might have resulted either from the inhibition of TG synthesis in liver or increased peripheral clearance of TG by stimulating LPL or inhibition of dietary cholesterol absorption from the intestine. The calories in excess of the requirement of the normal animal or man are known to be stored in the adipose tissue. The LPL (lipoprotein lipase) and HSL (hormone sensitive lipase) of the adipose tissue responsible for the uptake of triglycerides and mobilization in the fed and starved states respectively and skeletal muscle LPL seem to determine the level of

Table 1
Effect of twenty four weeks treatment of Potash alum on body weight, hemoglobin, blood glucose, lipid profile and teeth size of HFD fed rats

Treatment	Body weight (gm)		Blood glucose (mg/100ml)		Hemoglobin (g/100ml)	TC (mg/g)	TG (mg/g)	HDL (mg/g)	Teeth size (cm)
	Initial	Final	Initial	Final					
Normal control	200.32±6.23	210.12±4.65^c	85.33±3.87	86.45±1.324^c	10.45±0.11	46.67±1.56	36.47±3.45	31.33±2.21	1.44±0.61
Disease control	192.43±3.74	321.33±9.98^c	82.23±2.34	110.43±2.34^c	11.45±0.01^c	160.50±3.45	175.67±2.67	15.33±0.88	1.52±0.53
Prophylactic	188.66±5.56	302.34±8.89^b	75.76±2.31	95.52±3.34^c	12.61±0.88^c	120.27±2.78^c	155.54±4.68^c	17.44±0.61^b	3.02±0.43^c
Therapeutic	201.76±4.56	280.54±7.78^c	87.45±1.56	92.22±2.34^c	13.22±0.32^c	135.23±2.43^c	162.22±4.12^c	15.44±1.61^c	2.70±0.23^c
Alum+Obese	193.45±9.34	243.45±5.67^c	86.30±2.11	86.34±1.34^c	12.68±1.11^c	105.66±4.67^c	125.34±5.34^c	18.55±1.71^c	3.12±0.14^b
Alum control	199.47±6.67	179.98±8.57^c	82.34±1.23	87.45±3.44^c	11.11±0.13^c	48.23±3.61^c	46.47±1.19^c	28.12±1.34^c	3.16±0.23^c
4^c									

Data are expressed as Mean ± S.E.M. Where n=6. a. P<0.05; b. P<0.01; c. P<0.001 compared to HFD fed control (one way ANOVA followed by Tukey's post-test).

Table 2

Effect of nine weeks treatment of Potash alum on Liver enzyme profile, food intake, dry weight of feces and fecal lipid contents of HFD fed rats

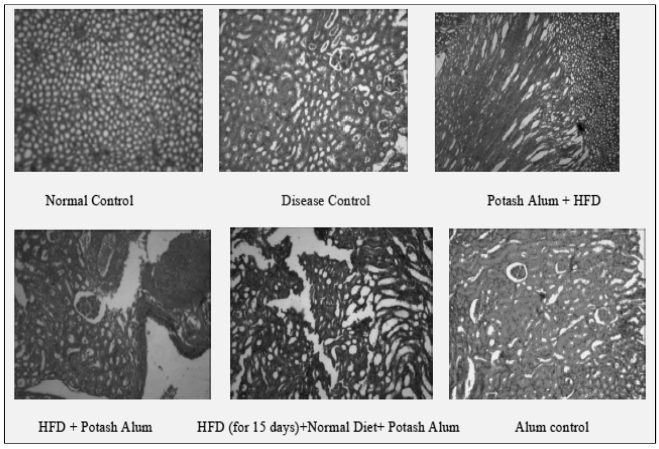
Treatment	ALP (mg/100ml)	TP (mg/100ml)	SGPT (mg/100ml)	SGOT (mg/100ml)	Albumin (mg/100ml)	Total bilirubin (mg/100ml)	Average food (g/week)	Dry weight of feces (g)	Fecal lipids (mg/g)
Normal control	47.17±1.51[b]	7.51±0.41[c]	65.52±2.11[c]	153.32±3.14[a]	3.22±0.71[c]	0.16±0.01[a]	15.71±1.23	1.52±0.13	110.2±3.70
Disease control	49.67±1.30	7.52±1.07	75.62±1.38	156.32±2.44[c]	3.83±0.29[c]	0.24±0.01[c]	20.23±1.24	3.42±0.23	129.3±3.20
Prophylactic	68.37±2.12[c]	8.11±1.11[b]	81.32±0.91[b]	155.33±2.56[c]	3.45±0.75[c]	0.36±0.11[c]	14.27±1.43[c]	1.85±0.25[c]	145.2±2.31[b]
Therapeutic	81.68±2.30[c]	7.12±1.13[c]	85.52±2.63[c]	162.22±1.18[c]	3.62±0.41[c]	0.23±-0.01[c]	15.53±2.73[a]	2.03±0.19[c]	152.3±3.6[c]
Alum+Obese	75.67±2.67[c]	8.18±1.08[c]	179.33±1.32[c]	165.23±4.15[b]	3.83±0.79[c]	0.65±0.17[c]	15.53±1.73[c]	2.03±0.19[b]	165.3±2.7[c]
Alum control	48.23±3.61[c]	7.17±0.15[c]	94.44±3.47[c]	185.53±3.98[c]	3.23±0.77[c]	0.32±0.04[c]	13.23±0.75[c]	1.51±0.18[c]	105.4±4.6[ns]

Data are expressed as Mean ± S.E.M. Where n=6. a. P<0.05; b. P<0.01; c. P<0.001 compared to HFD fed control (one way ANOVA followed by Tukey's post-test).

serum triglycerides. A related aspect is the role of substrate cycle between TG and FFA between adipose tissue and liver in determining TG levels in liver, serum and adipose tissue (6).

Figure 2

Photomicrographs of histopathological studies of kidneys of various groups stained with haematoxylin and eosin



Another possible mechanism that explains the low serum levels of TG in the Potash Alum treated groups might be the inhibition of pancreatic lipase or binding of TG that would have increased fecal excretion. The administration of Potash Alum for 24 weeks resulted in a significant reduction in serum TG, TC and increased HDL level indicating their hypolipidemic activity.

Toxicity study revealed that there was a significant increase in the size of teeth of Alum + Obese and Alum control groups. As far as our knowledge is concerned no prior publications has reported such kind of toxicity associated with alum. The exact mechanism of enlargement of teeth is not clear. However, it may be due to excess deposition of Ca2+ ions or Al3+ ion in the root of teeth. Increased SGPT, SGOT and ALP indicate the impending hepatotoxicity of Potash Alum (Table 2). Further, histopathological examination of kidney reveals antiobesity effect of potash alum (Fig. 2). An extensive research is required to decide the therapeutic dose and dosage formulation, with site specific dosage delivery in order to reduce the associated toxicities.

Conclusion

The present study provides clear evidence that Potash Alum is helpful in treating the HFD induced obesity. Anti-obesity action of Potash Alum in experimental animals may be partly mediated through delaying the intestinal absorption of dietary fat by inhibiting pancreatic lipase activity. Moreover, it might help in preventing obesity complications and serve as good adjuvant in the present armamentarium of anti-obesity drugs. However, toxicities associated with usage of Potash Alum is a major concern that has to be taken into account for that elucidation of mechanism of toxicities, drug modulation, selection of drug delivery and dosage form, on-site targeting and dose titration is a prerequisite.

References

1. West F, Sanders MR. The Lifestyle Behaviour Checklist: a measure of weight-related problem behaviour in obese children. Int J Pediatr Obes. 2009;4(4):266-73.
2. Yokel RA, Rhineheimer SS, Brauer RD, Sharma P, Elmore D, McNamara PJ. Aluminum bioavailability from drinking water is very low and is not appreciably influenced by stomach contents or water hardness. Toxicology 2001;161:93–101.
3. Gunse B, Poschenrieder C, Barcelo J. Water transport properties of roots and root cortical cells in proton- and Al-stressed maize varieties. Plant Physiol 1997;113:595–602.
4. Zhang HL, Yuan C, Zhang DM, Shi HS, LI M, Luo ZC, Wan Y, Lu L, Luo ST, Yang L. A novel combined conjugate vaccine: enhanced immunogenicity of bFGF with CRM197 as a carrier protein. Mol Med Report. 2011 Sep-Oct;4(5):857-63.
5. Srinivasan K, Patole PS, Kaul CL, Ramarao P. Reversal of glucose intolerance by pioglitazone in high-fat diet fed rats. Experimental and Clinical Pharmacology 2004; 26: 327-33.
6. Newsholme, E.A., Crabtree, B., 1976. Substrate cycles in metabolic regulation and in heat generation. Biochemical Society Symposia 41, 61-110.