ASSESSMENT OF THE SAFETY OF USE OF CERTAIN NATURAL ANTI-INFLAMMATORY AGENTS AND THEIR EFFECTS ON NUTRITIONAL STATUS IN ADULT AND GROWING RATS

SAHAR Y. AL-OKBI*
NAGWA M. AMMAR**
DOHA A. MOHAMED*

SUMMARY: The objective of the present study is the determination of the safety of use of some natural agents proved previously to have a remarkable anti-inflammatory activity. So screening of certain biochemical and nutritional changes that may occur on administration of the natural anti-inflammatory agents and two reference anti-inflammatory drugs was carried out in both adult and growing rats. The natural agents undertaken in this study were the petroleum ether and the alcoholic extracts of fenugreek seeds and liquorice roots and the whole powder of coriander fruits (200 mg/kg). The reference drugs used are indomethacin and urbason retard (5 mg/kg). In the first experiment, the natural or synthetic anti-inflammatory agents were given as daily oral dose to different groups of normal adult rats for a month. At the end of the experiment the serum total protein, albumin, ALP, AST, ALT, creatinine, BUN, glucose, cholesterol, Ca, P, Fe and TIBC were determined. Nutritional parameters (such as food intake, body weight changes and food efficiency ratio) were assessed. The biochemical and nutritional parameters were compared with control rats given no medications. Results showed non-significant changes of any of the studied biochemical parameters after the administration of the natural agents. However urbason retard produced significant increase of serum albumin and ALT and significant decrease of serum globulin. Concerning nutritional parameters, petroleum ether extract of liquorice and urbason retard produced significant reduction of body weight gain and total food intake. Food efficiency ratios were reduced significantly on the administration of urbason retard.

In the second experiment, nutritional status of growing rats fed balanced diet (10% casein) was assessed after 4 weeks of daily oral treatment with previously mentioned natural agents and reference drugs. Results showed significant increase of haematocrit on administration of either alcoholic or petroleum ether extract of liquorice. Alcoholic extract of fenugreek produced significant increase of haematocrit also while urbason retard produced significant increase in both haematocrit and haemoglobin. Serum total protein levels were significantly reduced on oral administration of urbason retard, indomethacin, petroleum ether or alcoholic extract of fenugreek, serum albumin was also significantly reduced on administration of the previous medication except in case of indomethacin. Urbason retard produced severe reduction of all the nutritional parameters including protein efficiency and food efficiency ratios. Petroleum ether extract of liquorice produced only significant reduction in protein and food efficiency ratios.

The third experiment was carried out aiming at improving the adverse effects occurring in serum protein of growing rats during the second experiment, through feeding high protein diet (20% casein). It was then observed that the serum protein levels in all the tested groups were maintained at normal levels.

Key Words: Indomethacin, urbason retard.

Table 1: Composition of diet (g/100 g).

Diet ingredients	Balanced diet	High protein diet
Casein, vitamin and fat free	10	20
Palm oil	10	10
Sucrose	25.17	21.83
Maize starch	50.33	43.67
Salt mixture (3)	3.5	3.5
Vitamin mixture (4)	1	1
Total	100	100

INTRODUCTION

In previous researches (1,2) it has been proven that the petroleum ether and alcoholic extracts of fenugreek seeds and liquorice roots as well as the whole powder of coriander fruits possess an anti-inflammatory activity in both acute and chronic inflammation. So it was of importance to determine the safety of use of these for mentioned natural agents and to study how these agents may affect nutritional status in adult and growing stages in comparison to synthetic anti-inflammatory agents.

The aim of the present research is to study the effect of daily oral administration of petroleum ether and alcoholic extracts of fenugreek and liquorice as well as the whole coriander fruits' powder on serum glucose, cholesterol, total protein, albumin, globulin, calcium, phosphorus, iron, total iron binding capacity, aspartate transaminase, alanine transaminase, alkaline phosphatase, creatinine and blood urea nitrogen on normal adult rats in comparison to synthetic anti-inflammatory drugs. In addition to studying their effect on body weight, food efficiency ratio in adult and growing rats and protein efficiency ratio, serum proteins, blood haemoglobin and haematocrit in growing rats.

*From Department of Food Sciences and Nutrition, National Research Centre, Dokki, Cairo, Egypt.
**From Department of Pharmaceutical Sciences, National Research Centre, Dokki, Cairo, Egypt.

MATERIALS AND METHODS

Animals

Male adult white albino rats of average body weight of 125.5 g were used in the first experiment. In the second and third experiments male and female growing rats of 49.5 g average weight were used. The animals were kept individually in wire bottomed cages at room temperature of 25 ± 2°C and a relative humidity of about 55%.

Drugs

Two reference anti-inflammatory drugs were used in the present study. Indomethacin [1-(4-chlorobenzoyl-5-methoxy-2- methylindol-3yl) acetic acid] as a non-steroidal drug and urbason retard (Methyl prednisolon) as a steroidal drug.

Diets

A balanced and a high protein diets (Table 1) were fed to rats during the experiments.

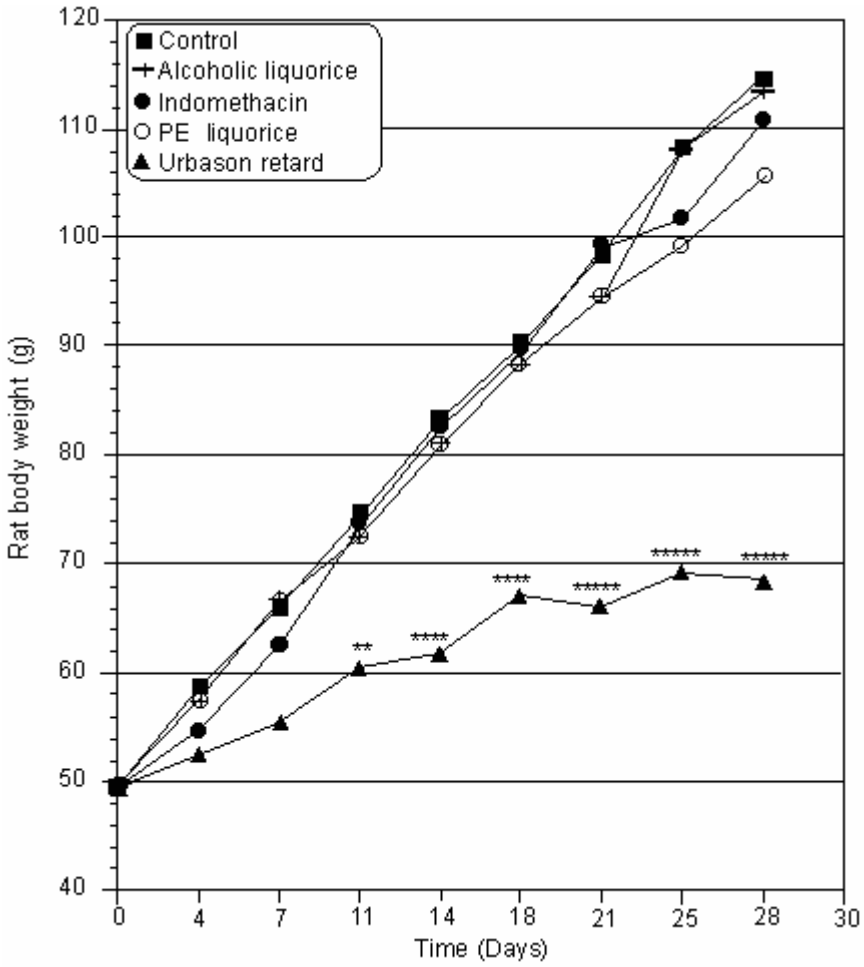
Plants' extracts (The source of natural anti-inflammatory agents)

Dried petroleum ether and alcoholic extracts of fenugreek seeds and liquorice roots as well as the whole powdered coriander fruits were used in our study.

Preparation of plant extract

500 g of the dried powder of each plant under investigation were placed in a continuous extraction apparatus and subjected to successive extraction using petroleum ether (60-80°C), then 50% aqueous methanol. The solvent of each extract was removed by distillation under reduced pressure at a temperature not exceeding 40°C and dried to a constant weight in a vacuum dessicator over anhydrous calcium chloride.

Figure 1: Growth curves of growing rats fed balanced diet and given daily dose of alcoholic or petroleum ether extract of liquorice (200 mg/kg) or the two reference anti-inflammatory drugs (5 mg/kg) and of control rats given no medication for 4 weeks.



Values significantly differ from the control: **p<0.025, ****p<0.005, *****p<0.001.

Preparation of the plants and drug doses

The dry alcoholic extracts of fenugreek and liquorice were dissolved in distilled water. The dry petroleum ether extracts of fenugreek, liquorice and the whole coriander fruits powder as well as indomethacin were suspended in distilled water using gum acacia. Urbason retard was ground and suspended in water without a suspending agent. The vehicle (gum acacia in water) was given to control adult rats. Natural agents were given as 200 mg/kg rat body weight. Synthetic drugs were given as 5 mg/kg rat body weight (5,6).

Design of experimental work

First experiment

The adult rats were divided into 9 groups each comprised of six rats. Five test groups were given daily oral dose of different natural agents and two reference groups were given the two synthetic drugs separately. Two control groups were run where no medications were given and one of them was given only daily oral dose of the vehicle. The experiment lasted for one month, during the whole experiment the rats were fed the balanced diet (Table 1). During the experimental period food intake and body weight of rats were measured twice weekly. After elapsing of the experimental period, total food intake, body weight variation and food efficiency ratio were calculated and tabulated.

At the end of the experiment, rats were fasted for 16 hours then the blood samples were drawn from eye vein orbitals. The blood samples were collected without anticoagulant, the sera were separated by centrifugation at 3000 r.p.m. for 15 minutes. The sera thus obtained were used for the determina-

Table 2: Serum biochemical parameters of adult rats fed balanced diet on daily oral administration of the different anti-inflammatory natural agents (200mg/kg) or the two reference anti-inflammatory drugs (5mg/kg) and of control rats for a month.

Groups		Glucose mg /100 ml	Cholesterol mg /100 ml	T. Protein g/100 ml	Albumin g/100 ml	Globulin g/100 ml	Albumin/Globulin	Creatinine mg/dl	BUN mg/dl	ALP U/L	AST U/ml	ALT U/ml	Ca mg/100 ml	P mg/100 ml	Fe µg/dl	TIBC µg/dl
Control	Mean	112.359	112.191	6.671	3.832	2.836	1.375	1.417	12.264	215.711	145.333	56.667	8.382	8.116	163.895	375.87
	± S.E.	2.211	8.239	0.209	0.044	0.177	0.073	0.069	0.487	12.142	3.422	1.282	0.772	0.446	15.153	3.355
Alcholic ext.of liquorice	Mean	114.458	97.225	7.539	4.355	3.185	1.392	1.536	9.911	193.589	156.833	60.667	9.943	8.227	143.563	400.881
	± S.E.	8.700	8.389	0.803	0.519	0.338	0.130	0.141	1.022	12.117	6.047	1.961	0.274	0.513	11.882	34.985
Alcholic ext.of fenugreek	Mean	113.363	97.767	7.134	4.247	2.888	1.499	1.805	10.303	250.308	161.833	66.333	7.035	7.846	173.815	389.869
	± S.E.	5.007	4.533	0.427	0.432	0.214	0.232	0.201	1.194	13.607	10.734	6.243	1.410	0.692	32.766	19.718
Urbason retard	Mean	103.700	91.691	7.593	4.903*	2.690*	1.908	1.629	14.767	190.383	161.007	70.5 *	8.274	7.581	181.665	451.338**
	± S.E.	20.285	16.542	0.659	0.429	0.312	0.214	0.094	1.473	10.210	13.256	5.982	0.803	0.550	34.330	23.737
Control (gum)	Mean	109.578	99.676	6.761	3.937	2.825	1.529	1.349	11.421	204.833	161.533	56.667	8.706	7.722	178.344	435.624
	± S.E.	10.189	12.487	0.281	0.109	0.295	0.272	0.111	1.269	14.569	12.022	4.863	0.679	0.598	31.675	40.439
PE ext.of liquorice	Mean	117.527	116.241	7.578	4.404	3.127	1.651	1.934	11.599	209.353	161.5	56	8.224	7.286	171.609	419.912
	± S.E.	3.104	15.531	0.869	0.421	0.526	0.356	0.247	2.049	6.507	10.645	3.724	1.285	0.623	16.280	30.748
PE ext.of fenugreek	Mean	110.918	106.507	7.759	4.291	3.469	1.469	1.544	8.681	238.865	155.333	58.167	9.823	7.128	177.021	414.170
	± S.E.	9.948	17.858	0.539	0.535	0.509	0.347	0.136	0.700	13.736	9.106	5.576	0.174	0.760	19.414	28.938
Coriander fruits powder	Mean	111.170	132.734	7.924	4.933	2.991	1.773	1.702	14.140	179.156	169.567	53.333	8.749	8.222	170.54	483.638
	± S.E.	5.395	22.313	0.883	0.490	0.447	0.236	0.190	1.013	7.507	12.917	5.993	0.745	0.837	27.855	21.924
Indomethacin	Mean	115.369	94.139	7.349	4.273	3.077	1.534	1.559	11.537	180.746	153.333	58.333	7.152	6.624	186.745	510.802
	± S.E.	7.571	6.228	0.5914	0.281	0.435	0.247	0.132	1.731	5.593	13.306	6.075	0.625	0.221	20.499	26.051

Values significantly differ from the control: *p<0.05, **p<0.025.

tion of glucose (7), cholesterol (8), aspartate transaminase (AST) (9), alanine transaminase (ALT) (9), alkaline phosphatase (ALP) (10), creatinine (II), blood urea nitrogen (BUN) (12), phosphorus (13), calcium (14), iron (15), total iron binding capacity (TIBC) (16), total protein (17) and albumin (18). Serum globulin concentration was calculated by subtracting the albumin concentration from total protein concentration.

Second experiment

This experiment was done for determination of protein efficiency ratio and nutritional status during administration of natural and synthetic anti-inflammatory agents in growing rats.

The rats were divided into 8 groups each including six rats. Five test groups were given the different natural agents while the two reference groups were given the two synthetic drugs separately as daily oral dose. A control group, where rats received no medications, was run. The experiment continued for four weeks. Rats were maintained on balanced diet throughout the experiment. During experimental period, food intake and body weight of rats were determined twice weekly. Growth curves were drawn representing the relationship between the body weight and time. At the end of experiment, total food intake, body weight variation, food efficiency ratio, and protein efficiency ratio were calculated and tabulated. Rats were fasted 16 hours then blood samples were drawn from eye vein orbital for determination of haematocrit (19) and hemoglobin (2). Another part of blood samples were collected on heparin; plasma was separated by centrifugation at 3000 r.p.m. for 15 minutes. Plasma was used for the determination of total proteins and albumin. Globulin concentration was calculated as in the previous experiment.

Third experiment

From the results of the previous experiment on growing rats we noticed that fenugreek extracts, indomethacin, and urbason retard produced unwanted effects on plasma pro-

Table 3: Nutritional parameters of adult rats fed balanced diet on oral administration of the different anti-inflammatory natural agents (200mg/kg) or the two reference anti-inflammatory drugs (5mg/kg) and of control rats for a month.

Groups		Initial body weight (g)	Final body weight (g)	Body weight variation (g)	Total food intake (g)	Food efficiency
Control	Mean	125.5	202.833	77.333	483.4	0.160
	± S.E.	4.342	8.142	4.602	10.806	0.009
Alcoholic ext.	Mean	125.667	196.5	70.833	472.783	0.149
of liquorice	± S.E.	0.667	4.709	5.009	13.591	0.008
Alcoholic ext.	Mean	125.5	201.833	76.333	491.417	0.155
of fenugreek	± S.E.	1.586	7.481	6.667	19.278	0.011
Urbason	Mean	125.5	170.333****	44.833****	446.383**	0.100*****
retard	± S.E.	2.217	3.383	2.496	4.884	0.005
Control	Mean	125.5	206.0	80.5	479.85	0.167
	± S.E.	2.802	6.851	4.808	11.636	0.007
PE ext. of	Mean	125.5	188.5	63.0*	426.193**	0.147
liquorice	± S.E.	1.088	5.614	4.851	15.255	0.008
PE ext. of	Mean	125.5	193.333	67.833	463.317	0.144
fenugreek	± S.E.	2.277	8.751	6.935	22.037	0.009
Coriander	Mean	125.833	188.833	63.00	453.883	0.136
fruits powder	± S.E.	1.046	9.955	9.427	22.556	0.013
Indomethacin	Mean	125.5	175.0	49.5	418.567	0.105
	± S.E.	4.169	17.614	15.392	48.853	0.024

Values significantly differ from the control; *p<0.05, **p<0.025, ****p<0.005, *****p<0.001.

teins. The following experiment was therefore carried out as a trial to improve these effects.

Male and female growing rats were divided into five groups each comprised of six rats. One control group and five test groups. The rats of the control group were fed the balanced diet. Two test groups of rats, the rats of each group were given daily oral dose of 200 mg of either alcoholic or petroleum ether extract of fenugreek/kg rat body weight. Two reference groups of rats, the rats of each group were given daily oral dose of 5 mg of either indomethacin or urbason retard/kg rat body weight. The rats of test and reference groups were fed high protein diet (20%) (Table 1) all through the experiment.

The experiment continued for four weeks, at the end of which rats were fasted 16 hours then blood samples were drawn from eye vein orbital and the same blood analyses of the second experiment were carried out.

Statistical analyses of the results were carried out using Student's t test.

RESULTS AND DISCUSSION

The biochemical results of the adult rats (first experiment) are shown in Table 2. In our study, non-significant changes on serum total protein, albumin and globulin were noticed on administration of any of the natural agents or indomethacin. On administration of urbason retard total serum protein was not significantly affected whereas serum albumin increased and globulin decreased significantly. It was reported by Tietz (16) that administration of corticosteroids results in an

Table 4: Biochemical parameters of growing rats fed balanced diet on daily oral administration of the different anti-inflammatory natural agents (200mg/kg) or the two reference anti-inflammatory drugs (5mg/kg) and of control rats given no medication for 4 weeks.

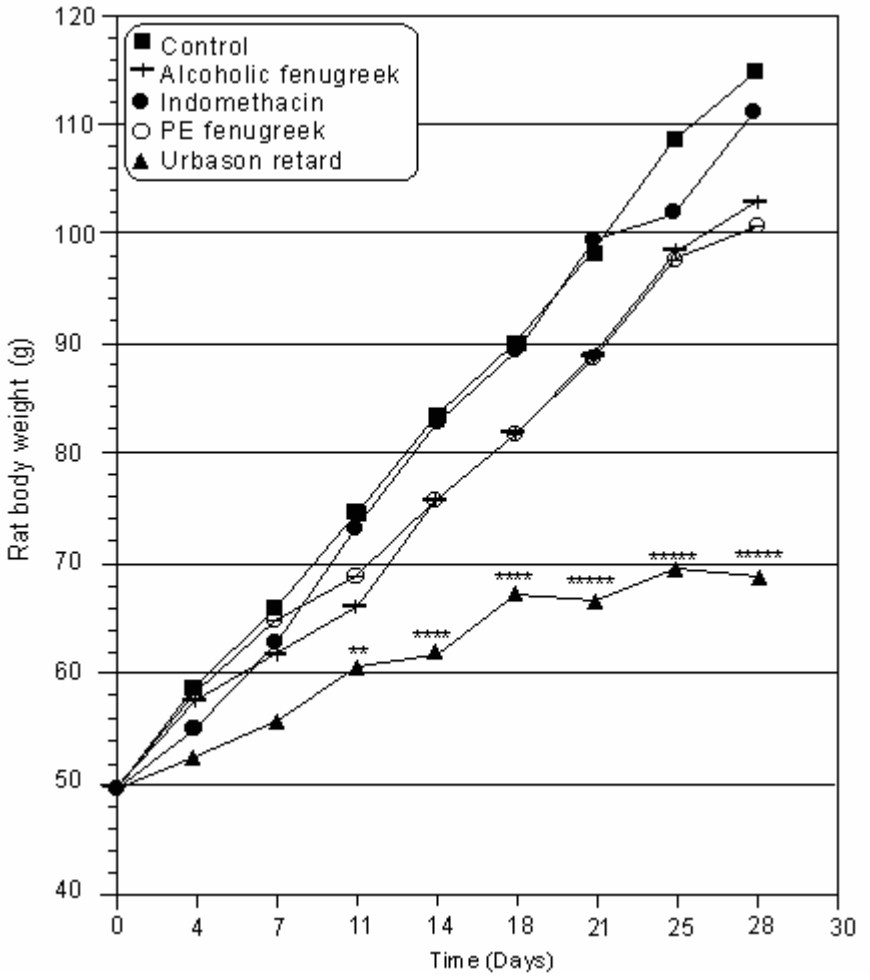
Groups	Time (hours)						
		Haematocrit %	Hemoglobin mg/100 ml	T. protein g/100 ml	Albumin g/100 ml	Globulin g/100 ml	Albumin/ Globulin
Control	Mean	44.167	12.324	7.160	3.778	3.382	1.128
	± S.E.	0.543	0.536	0.243	0.077	0.182	0.042
Alcoholic ext. of liquorice	Mean	48.333*	12.329	7.527	4.061	3.466	1.19
	± S.E.	1.667	0.193	0.098	0.182	0.131	0.103
	% increase	9	-	-	-	-	-
PE ext. of liquorice	Mean	49.167*****	13.682	7.488	4.106	3.472	1.167
	± S.E.	0.909	0.318	0.176	0.189	0.108	0.083
	% increase	11	-	-	-	-	-
Alcoholic ext. of fenugreek	Mean	47.167**	12.679	6.008****	3.159****	2.848	1.166
	± S.E.	1.515	0.286	0.209	0.265	0.244	0.149
	% decrease	-	-	16	16	-	-
PE ext. of fenugreek	Mean	47.00	13.629	6.328**	3.342*****	2.986	1.125
	± S.E.	1.342	0.374	0.109	0.041	0.099	0.039
	% decrease	-	-	12	12	-	-
Indomethacin	Mean	45.167	13.486	5.757****	3.201	2.539**	1.361
	± S.E.	1.621	0.322	0.204	0.206	0.259	0.201
	% change	-	-	20	-	25	-
Urbason retard	Mean	51.833*****	14.619****	5.735*****	3.029***	2.706**	1.157
	± S.E.	0.543	0.144	0.136	0.199	0.174	0.126
	% increase	17	19	20	20	20	-
Control	Mean	45.167	13.795	6.122	3.461	2.662	1.353
	± S.E.	0.654	0.283	0.244	0.171	0.199	0.167
Coriander fruits powder	Mean	41.5	13.783	6.164	3.417	2.747	1.280
	± S.E.	1.839	0.432	0.099	0.147	0.165	0.128

Values significantly differ from the control; *p<0.05, **p<0.025, ***p<0.010, ****p<0.005, *****p<0.001.

increase in serum protein levels and in circulating amino acids. They have an anabolic effect on protein in liver (increase total protein synthesis) and an adverse effect in the peripheral tissues (muscle, adipose and lymphoid tissue) where they have catabolic effect since, protein synthesis is depressed, and the degradation increased.

Serum creatinine, blood urea nitrogen, alkaline phosphatase, and transaminases were not affected when any of the natural agents or the non steroidal

Figure 2: Growth curves of growing rats fed balanced diet and given daily oral dose of alcoholic or petroleum ether extract of fenugreek (200 mg/kg) or the two reference anti-inflammatory drugs (5 mg/kg) and of control rats given no medication for 4 weeks.

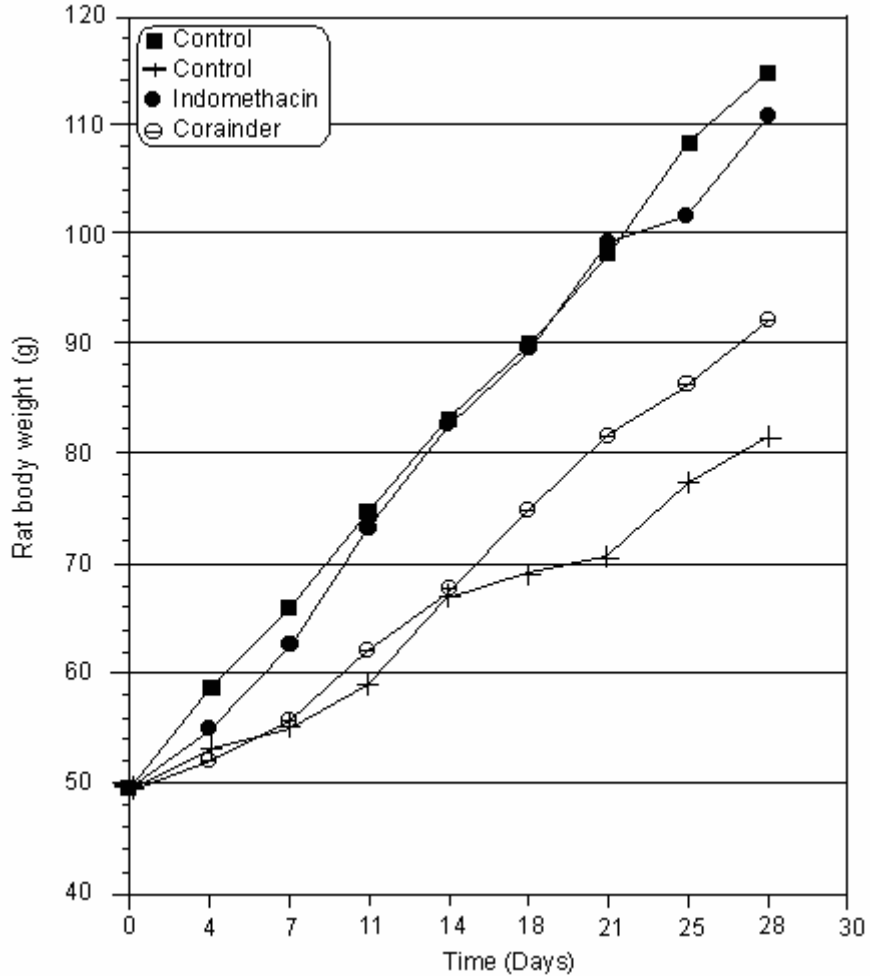


Values significantly differ from the control: **p<0.025, ****p<0.005, *****p<0.001.

anti-inflammatory drugs were administered in our study. Administration of urbason retard produced significant increase of serum ALT. It was reported by Tietz (16) that although serum levels of both AST and ALT become elevated whenever disease process or lesions affect liver cell integrity, serum elevations of ALT are rarely observed except in parenchymal liver disease and lesions. Moreover, elevations of ALT activity persist longer than do those of AST activity.

The natural anti-inflammatory agents and reference drugs produced non-significant changes on fasting blood sugar and cholesterol in our study. However hyperglycemia was reported by some authors on administration of steroidal anti-inflammatory drugs (21). Hyperglycemia usually occur during the later period of treatment (22). It was reported by some authors that high glucose tolerance curve occurs only on administration of large doses of steroidal anti-

Figrue 3: Growth curves of growing rats fed balanced diet and given daily oral dose of coriander fruits powder (200mg/kg) or indomethacin (5 mg/kg) and of control rats given no medication for 4 weeks.



inflammatory drugs in normal individuals (23).

Fenugreek seeds were reported to have anti-diabetic and hypocholesterolemic effects (24). The anti-diabetic and hyper cholesterolemic effects were suggested to be due to presence of galactomannan and saponins (25,26). This means that the effect resides in the alcoholic extract of fenugreek. Glycyrrhizin, the main active constituent of alcoholic extract of liquorice, was reported to have hypocholesterolemic effect. Some authors (27,28) proved that coriander possess anti-diabetic activity in human and experimental diabetic animals. These literature were not in agreement with our results which might be due to the fact that our study was done on normal rats, these effects may be more prominent in hypercholesterolemic and hyperglycemic subjects.

Serum calcium, phosphorus, iron and iron binding capacity show some abnormalities in chronic inflammatory diseases such as rheumatoid arthritis (29). So it is worthy to know to what extent they will be modified by the natural anti-inflammatory agents and reference drugs in our study. The results showed that their serum levels did not show any significant changes on administration of any of the anti-inflammatory agents used in

Table 5: Biochemical parameters of control growing rats fed balanced diet and growing rats fed high protein diet on oral administration of alcholic or petroleum ether extract of fenugreek (200 mg/kg) and the two reference anti-inflammatory drugs (5 mg/kg) for 4 weeks.

Groups	Time (hours)						
		Haematocrit %	Hemoglobin mg/100 ml	T. protein g/100 ml	Albumin g/100 ml	Globulin g/100 ml	Albumin / Globulin
Control	Mean	44.667	12.555	6.785	3.464	3.320	1.099
	± S.E.	0.615	0.196	0.328	0.133	0.335	0.124
Alcoholic ext. of fenugreek	Mean	44.833	12.365	8.354	4.110	4.243*	0.986
	± S.E.	1.046	0.344	0.369	0.345	0.217	0.102
PE ext. of fenugreek	Mean	43.5	12.875	7.267	3.775	2.992	1.592
	± S.E.	0.428	0.729	0.317	0.569	0.365	0.288
Indomathacin	Mean	45.167	12.508	8.434	4.246	4.188	1.035
	± S.E.	0.477	0.389	0.350	0.304	0.262	0.092
Urbason retard	Mean	43.333	13.285	7.169	3.313	3.857	0.874
	± S.E.	1.358	0.449	0.222	0.078	0.213	0.061

Values significantly differ from the control; *p<0.05.

our study. However urbason retard produced significant increase of total iron binding capacity.

The results of nutritional parameters of the first experiment are shown in Table 3. Administration of urbason retard or petroleum ether extract of liquorice produced significant decrease of body weight gain and total food intake. This decrease was not sufficient to produce reduction of food efficiency ratio in case of petroleum ether extract of liquorice. However food efficiency ratio decreased significantly on administration of urbason retard. Administration of fenugreek extracts, alcoholic extract of liquorice or whole powdered coriander fruit as well as indomethacin produced no changes in nutritional parameters. It was reported by Swanston *et. al.* (27) that, in normal mice, food intake, body weight gain were not affected by 12 day of treatment with coriander.

The biochemical results of the second experiment are shown in Table 4. The percentage haematocrit was significantly increased on administration of either alcoholic or petroleum ether extract of liquorice and alcoholic extract of fenugreek in case of rats fed balanced diet. Administration of urbason retard produced significant increase in both percentage haematocrit and hemoglobin concentration which might be due to increased total white blood cells, red blood cells and platelets on administration of steroidal anti-inflammatory drugs reported by Ganong (30). The effect on percentage haematocrit on administration of alcoholic extract of liquorice and fenugreek may be related to the presence of corticosteroidal like substance in the extract such as glycyrrhetinic acid salt (31) and sapogenins (32) respectively.

Serum total protein levels were significantly reduced in growing rats fed balanced diet on oral administration of urbason retard, indomethacin, petroleum ether or alcoholic extract of fenugreek for 28 days. This decrease is mainly due to reduction of albumin in case of petroleum ether and alcoholic extract of fenugreek, and to globulin in case of indomethacin and

Table 6: Nutritional parameters of growing rats fed balanced diet on daily oral administration of the different anti-inflammatory natural agents (200 mg/kg) or the two reference anti-inflammatory drugs (5 mg/kg) and of control rats given no medication for 4 weeks.

Groups		Initial body weight (g)	Final body weight (g)	Body weight variation (g)	Total food intake (g)	Total food intake (g/day)	Total protein intake (g)	Food efficiency	Protein efficiency
Control	Mean	49.5	114.667	65.167	238.28	8.51	23.828	0.272	2.720
	± S.E.	2.717	7.570	5.782	14.474	0.517	1.447	0.013	0.132
Alcoholic ext. of liquorice	Mean	49.5	113.333	63.833	247.3	8.828	24.73	0.256	2.556
	± S.E.	2.291	5.759	6.167	13.706	0.489	1.371	0.012	0.125
PE ext. of liquorice	Mean	49.5	105.667	56.167	241.75	8.633	24.175	0.232*	2.322*
	± S.E.	1.857	4.177	3.301	8.629	0.308	0.863	0.009	0.099
Alcoholic ext. of fenugreek	Mean	49.5	102.5	53	224.417	8.017	22.442	0.237	2.374
	± S.E.	1.668	3.364	3.098	10.263	0.367	1.026	0.014	0.141
PE ext. of fenugreek	Mean	49.5	100.333	50.833	211.833	7.565	21.183	0.232	2.324
	± S.E.	1.176	8.535	8.308	16.845	0.602	1.684	0.025	0.254
Indomethacin	Mean	49.5	110.833	61.833	243.267	8.688	24.327	0.252	2.524
	± S.E.	2.884	5.350	4.030	14.615	0.522	1.462	0.009	0.096
Urbason retard	Mean	49.5	68.667*****	19.167*****	191.117**	6.83**	19.112**	0.096*****	0.965*****
	± S.E.	2.109	3.073	8.375	8.375	0.299	0.838	0.019	0.198
Control	Mean	49.167	84.667	35.5	215.367	7.692	21.537	0.163	1.637
	± S.E.	1.740	2.565	3.547	10.263	0.367	1.026	0.010	0.102
Coriander fruits powder	Mean	49.5	92.167	42.667	234.15	8.363	23.415	0.178	1.784
	± S.E.	0.619	6.549	6.407	22.244	0.794	2.224	0.014	0.142

Values significantly differ from the control; *p<0.05, **p<0.025, *****p<0.001.

to both albumin and globulin in case of urbason retard. It is worthy to mention that administration of urbason retard, indomethacin and petroleum ether and alcoholic extract of fenugreek to growing rats in the third experiment during feeding high protein diet (20%) in our study (Table 5) improved serum protein levels to nearly normal values.

The results of nutritional parameters of rats of the second experiment are represented by Table 6, growth curves are shown in Figures 1, 2 and 3. Urbason retard administration to growing rats produced significant reduction of body weight which started from the eleventh day of experiment till the last day. This decrease in body weight may be due to negative nitrogen balance resulted on administration of corticosteroids (21). Administration of either petroleum ether extract of liquorice or urbason retard to growing rats produced significant reduction of food and protein efficiency ratios. This reduction in case of urbason retard is four times that in petroleum ether extract of liquorice. No changes were noticed in nutritional parameters of growing rats on administration of fenugreek extracts, alcoholic extract of liquorice or whole powdered coriander fruit as well as indomethacin. It was reported by Shibata *et. al.* (33) that fenugreek produced no changes in weight gain and food and protein efficiency ratios of growing rats which is in agreement with our results.

Finally it can be concluded that the natural anti-inflammatory agents used in our study are safe to be used as remedy within the limits of our study specially concerning the biochemical parameters, however it is recommended to use high protein diet during the administration of petroleum ether and alcoholic

extracts of fenugreek in growing stage. Concerning the nutritional parameters, all natural agents used in our study did not produce any changes except the petroleum ether extract of liquorice which produced reduction in nutritional parameters in both growing and adult stages. Methyl prednisolon (urbason retard) was the worst medication used in our study concerning its effect on both biochemical and nutritional parameters.

REFERENCES

1. Ammar NM, AL-Okbi SY and Mohamed DA : Study of the anti-inflammatory activity of some medicinal edible plants growing in Egypt. J Islamic Academy of Sciences 10, 113, 1997.

2. Al-Okbi SY, Ammar NM, Abdel Samed AM, Rashed MM and Mohamed DA : Biochemical, nutritional and pharmacological evaluation of the anti-arthritic activity of some Egyptian plants. J Drug Res Egypt 22, 321, 1998.

3. Briggs GM and Williams MA : A new mineral mixture for experimental rat diets and evaluation of other mineral mixtures. Fed Proc 22, 261, 1963.

4. Morcos SR : The effect of protein value of the diet on the neurological manifestations produced in rats by b-immodipropionitrile. Br J Nutr 21, 269, 1967.

5. Amagaya S, Sugishita E, Ogihara Y, Ogawa S, Okada K and Aizawa T : Comparative studies of the anti-inflammatory activities of the stereoisomers of glycyrrhetinic acid. J Pharmacobio. Dyn 7, 923, 1984.

6. Ozaki Y, Mamoru N, Hiroyuki K and Mosatoshi H : Studies on concentration of glycerrhizin in plasma and its absorption after oral administration of licorice extract and glycyrrhizin. Yakugaku Zasshi. 110, 77, 1990.

7. Triender P : Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann Clin Biochem. 6, 24, 1969.

8. Watson D : A simple method for the determination of serum cholesterol. Clin Chem Acta 5, 637, 1960.

9. Reitman S and Frankel S : Colorimetric methods for determining GOT and GPT Am J Clin Path 28, 56, 1957.

10. Belfield A and Goldberg DM : Revised assay for serum phenyl phosphate activity using 4-amino- antipyrine. Enzyme 12, 561, 1971.

11. Houot O : Interpretation of clinical laboratory tests. Ed by G Henny J Siest, F Schiele, DS Young : Biomedical publications, 1985.

12. Fawcett JK and Scott JE : A rapid and precise methods for the determination of urea. J Clin Pathol 13, 156, 1960.

13. Taussky HH and Shorr E : A microcolorimetric methods for the determination of inorganic phosphorus. Enzyme 202, 675, 1953.

14. Gindler E, Melvin JD and King MD : Rapid colorimetric determination of calcium in biologic fluids with methyl thymol blue. Am J Clin Path 58, 367, 1972.

15. Stookey LL : Ferrozine a new spectrophotometric reagent for iron. Anal Chem 42, 779, 1970.

16. Tietz NW : In fundamentals of clinical chemistry. Saunders, Philadelphia, p 924, 1982.

17. Henry R : Clin. Chem. Principles and technics. Harper-Row New York p 182, 1964.

18. Doumas BT, Watson WA and Biggs HG : Albumin standards and the measurement of serum albumin with bromcresol green. Clin Chem Acta, 31, 87, 1972.

19. Vankampen EJ and Zijlstra WG : Determination of haemoglobin and its derivatives. Adv Clin Chem 8, 141, 1965.

20. Strumia MM, Sample AB and Hart ED : An improved microhaematocrite method. Am J Clin Path 221, 1016, 1954.

21. Dale MM and Foneman JC : Text Book of Immunopharmacology. First edition, printed in Great Britain by Butler and Tanner Lmt, USA, p 285, 1984.

22. Murray RK, Granner DK, Mayes PA and Rodwell VW: Harper's Biochemistry. Twenty-third edition, printed by Appleton and Lange, a publishing Division on Prentice Hall, p 688, 1993.

23. Joplin GF, Frazer R and Keeley KJ : Lancet 2, 67, 1961.

24. Sharma RD and Raghuram TC : Hyperglycemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. Nutr Res 10, 731, 1990.

25. Madar Z and Ilan S : Polysaccharide composition of gel function derived from fenugreek and its effect on starch digestion and bile acid absorption in rats. J Agric Food Chem 38, 1535, 1990.

26. Stark A and Madar Z : The effect of an ethanol extract derived from fenugreek (Trigonella foenum-graecum) on bile acid absorption and cholesterol levels in rats. Br J Nutr 69, 277, 1993.

27. Youness RI, Ahmed HH, Fayez M, Mansour SA and Soliman FA : The hypoglycemic effects of some commonly used plants and seeds. Zool Soc Egypt Bull 10, 121, 1985.

28. Swanston F, Day C, Bailey CJ and Flatt PR : Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetologia. 33, 462, 1990.

29. Golding DN : A synopsis of Rheumatic diseases. Fifth edition, printed and bound in England by Page bros, Ltd, Norwich, England, p 29, 1989.

30. Ganong FW : Review of medical physiolog. 8th edition, Lang medical publications, Los Altos, California, p 384, 1971.

31. Shibata S, Takahahi K, Yanc S, Harada M, Saito H, Tamura H, Kumagi A, Hirabayashi K, Yamamoto M and Nagata N : Chemical modification of glycyrrhetininc acid in relation to the biological activities. Chem Pharm Bull 5, 1910, 1987.

32. Pasich B, Terminska K and Beblot D : Disogenin and yamogenin in domestic Semen Foenugraect. Herba Pol 29, 203, 1983.

33. Shibata K, Murata K, Toguchi H and Shimabayshi Y : Effect of trigonelline on growth and DNA level of young rats. Teikoku Gakuen Kiyo, 10, 9, 1984.

Correspondence:
Sahar Y. Al-Okbi
Food Sciences and
Nutrition Department
National Research Centre,
Dokki, El Tahreer Street, Cairo,
EGYPT.
e-mail: S_Y_alokbi@hotmail.com