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Article

Daily Consumption of Honey: Effects on Male Wister Albino Rats

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Abstract: This study was primarily designed to investigate the effect of acute administration of honey on the biochemical parameters on male Wister albino rats. Fifteen male rats were divide into five groups of three each and were administered with distilled water, 10%, 20%, 50%, and 100% (v/v) of pure honey daily for seven days in that order. On the eighth day the rats were humanly sacrificed and blood samples were collected for analyses. Diastase activity and hydroxylmethylfurfural level were determined from the honey. Serum protein, albumin, globulin, glucose, urea, creatinine, alkaline phosphatase, alanine aminotransferase, total cholesterol, HDL, LDL, VLDL and complete blood counts were determined by automatic analyzer. Diastase activity and hydroxylmethylfurfural level were below the imposed limits. Significant ($p < 0.05$) increased in body weight was observed as the administration progressed days except on 1st and 2nd days at 20% (v/v). Also within the treatment group, the body weight increased in a concentration dependent manner from 10% to 20% but started decreasing from 50% to 100% (v/v). Significant ($p < 0.05$) decrease in creatinine level was observed from 20% to 100% (v/v). ALP and ALT activities dropped at 100% (v/v). However, significant ($p < 0.05$) decrease in triglyceride and VLDL were observed with simultaneous significant ($p < 0.05$) increase in packed cell volume, mean corpuscular hemoglobin and white blood cell counts at 20% (v/v) treated

group. The levels dropped with increasing concentration. Significant ($p < 0.05$) increase in platelet and decrease in mean cell volume as well as mean corpuscular hemoglobin concentration were observed in a concentration dependent manner. Results from this study suggest that daily consumption of honey might have some positive and negative effects on body weight, biochemical and hematological parameters, respectively.

Keywords: honey; male Wister albino rats; biochemical parameters; hematological parameters; body weight.

1. Introduction

Honey, a sweet food made by bees using nectar from flowers has been proven to be of medicinal importance both at curative and preventive levels. It is a promising antitumor agent with pronounced antimetastatic and antiangiogenic effects (Hanaa and Shynaa, 2011), antibacterial, anti-inflammatory, immune-stimulant, antiulcer and wound/burn healing (Fiorani *et al.*, 2006). Various signaling pathways, including stimulation of tumour necrosis factor-alpha (TNF-α) release, inhibition of cell proliferation, induction of apoptosis and cell cycle arrest, as well as inhibition of lipoprotein oxidation, mediate the beneficial effects exerted by honey and its major components such as chrysin and other flavonoids (Gheldof *et al*., 2002; Mabrouk *et al*., 2002; Swellam et al., 2003; Tonks *et al*., 2001; Woo *et al*., 2004). However, chronic consumption of honey that was mixed with rat pellets has been shown to have a positive impact on the architecture and integrity of hepatocytes *in vivo* (Wilson *et al.,* 2011). Its protective role against the kidney dysfunctions induced by sodium nitrite, a known food additives, hepatoprotective, hypoglycemic, reproductive, antihypertensive and of course antioxidant effects has also been reported (Hassan, 2007; Omotayo *et al.*, 2012). Honey is produced from many different floral sources and its biochemical and pharmacological activities vary depending on its origin and processing. Honey contains a variety of biologically active compounds such as flavonoids, vitamins, antioxidants as well as hydrogen peroxides (H_2O_2) (Mohammadzadeh *et al*., 2007). Although there have been a lot of progressive researches that have been conducted on honey, none has so far taken into cognizance of the possible effects of pure honey acute administration on heamatological and biochemical parameters. Therefore, this study was undertaken to investigate the effect of acute administration of honey on the heamatological and biochemical parameters on male Wister albino rats with a view to ascertain and validate whether it is safe to be taken honey on daily basis.

2. Materials and Methods

2.1. Sample Collection

Honey was collected from the northwest frontier of Pakistan (N.W.F.P) during spring season from *acacia* flower and maintained at 4^oC till analysis. All the chemicals and reagents used were of analytical grades.

2.2. Quality Assessment on the Honey Sample

To ensure the quality of the honey sample, diastase activity/diastase number (DN) and hydroxylmethylfurfural (HMF) level were determined using spectrophotometric method (AOAC, 2006) and briefly explained below.

2.2.1. Determination of hydroxylmethylfurfural (HMF)

Five grams of honey were dissolved in 25 mL of distilled water, treated with a clarifying agent (0.5 mL of Carrez I and 0.5 mL of Carrez II solutions) and volume made up to 50 mL. The solution was filtered, and the first 10 mL discarded. The absorbance of the filtered solution was measured at 284 and 336 nm against an aliquot of the filtered solution treated with $NaHSO_3$. HMF was determined as:

$$\text{mg of HMF/100g of honey} = (A_{284nm} - A_{336nm}) \times 14.97 \times 5/\text{g of test sample}$$

2.2.2. Diastase activity/number (DN)

Diastase activity was determined using a buffered solution of soluble starch and honey incubated in a thermostatic bath at 40^{o}C. Thereafter, 1 mL aliquot of this mixture was removed at 5 min intervals and the absorption of the sample was followed at 660 nm. The diastase value was calculated using the time taken for the absorbance to reach 0.235, and the results were expressed in Gothe degrees as the amount (mL) of 1% starch hydrolyzed by an enzyme in 1 g of honey in 1 h. The DN was calculated as follows:

$$\text{DN (units/g of honey)} = 28.2 \times \text{change in } A_{660nm} + 2.64$$

2.3. Animals

Fifteen male albino rats weighing 160 – 189 g were used for the present investigation. They were reared at the animal house of the International Center for Chemical and Biological Sciences, University of Karachi, Karachi, Pakistan with the approval of animal rights review committee. They were acclimatized for 1 week on normal diet of pelletized mouse chow, with water given *ad libitum* at room temperature within a 12-h light and dark cycle before the commencement of the experiment.

2.4. Experimental Design

The animals were divided into five different groups of three rats each according to their body weight proximity and treated daily for seven days as shown in Fig.1. Twenty-four hours after the last administration, animals were humanly sacrificed by using 60 mg/kg body weight of sodium pentothal. Blood samples were collected, part of the samples were placed in EDTA bottles for hematological analysis and the remaining were centrifuged at 4,000 rpm for 5 min to obtain the serum for analyses.

2.5. Determination of Biochemical and Hematological Parameters

The lipid profile, serum glucose, urea, creatinine, alkaline phosphatase (ALP), alanine aminotransferase (ALT), total protein, albumin and globulins were determined by using Auto Analyzer Hitachi Roche 7020 (902), Japan Inc. according to manufacturer's protocols. Complete blood counts were also determined using Coulter HmX Hematology Analyzer Beckman Coulter Inc. according to manufacturer's protocols.

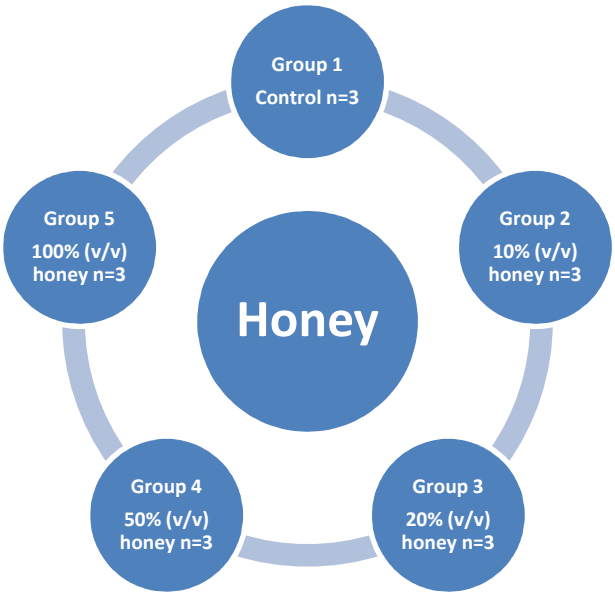

Figure 1: Experimental design.

2.6. Statistical Analysis

The results were expressed as mean ± standard error of the mean. Differences between the groups were analyzed by one-way analysis of variance (ANOVA) with the aid of Statistical Package for Social Sciences (SPSS) software, SPSS Inc., Chicago, Standard version 10.0.1. P-values < 0.05 were considered statistically significant for differences in mean using the least of significance difference (Lsd).

3. Results

The diastase activity and hydroxylmethylfurfural level were 2.7 units/g of honey and 0.44 mg/100 g of honey, respectively. This shows that the honey is of good quality as the values are far below the imposed limit of > 8 units/g of honey for DN and > 15 mg/100 g of honey for HMF (Muli *et al*., 2007). Table 1 shows the results of body weight of the experimental animals administered with honey. Significant ($p < 0.05$) increased in body weight was observed as the administration progressed except on 1st and 2nd days at 20% (v/v). Also within the treatment group, the body weight increased in a concentration dependent manner from 10% to 20% but started decreasing from 50% to 100% (v/v). There were no significant ($p < 0.05$) difference across the treatment groups based on the glucose and urea levels as depicted in Table 2. Significant ($p < 0.05$) decrease in creatinine level was observed from 20% to 100% (v/v) treated groups indicating protection on kidney. However, there was a significant ($p < 0.05$) increased in ALP and ALT activity in a concentration dependent manner, but surprisingly the activity dropped at 100% (v/v). The various treatment does not seem to have a significant ($p > 0.05$) effect on total protein, albumin, globulin and albumin/globulin ratio as shown in Table 3. Similarly, from Table 4, there were also no significant ($p > 0.05$) effects on cholesterol, HDL, LDL and cholesterol HDL ratio. However, significant ($p < 0.05$) decrease in triglyceride and VLDL were observed, indicating the fact that the treatments might not be having lipogenic effects. Table 5 shows the effect on heamatological parameters. No significant ($p > 0.05$) effect on Hb and RBC were

observed with concomitant significant ($p < 0.05$) increased in PCV, MCH and WBC at 20% (v/v) treated group. However, the levels dropped with increasing concentration. Significant ($p < 0.05$) increase in PLT, decrease in MCV and MCHC were observed in a concentration dependent manner.

Table 1: Results of body weight of rats administered with honey for a period of one week

Group	Treatment	Initial body weight	Days						
			1st	2nd	3rd	4th	5th	6th	7th
1	distilled	164.0	187.7	197.0	205.3	208.3	211.7	213.0	220.0
	water	± 2.8	± 2.9*	± 3.2*	± 5.5*	± 5.8*	± 6.2*	± 6.7*	± 7.5*
2	10 %	178.3	194.3	206.7	208.3	209.7	213.3	215.7	218.3
	(v/v)	± 4.9	± 4.9*	± 4.8*	± 3.2*	± 4.4*	± 5.4*	± 5.6*	± 4.4*
3	20 %	189.7	211.0	218.7	229.7	230.0	235.3	238.0	239.7
	(v/v)	± 4.3	± 9.2	± 10.5	± 9.9*	± 10.2*	± 9.7*	± 11.1*	± 12.3*
4	50 %	174.0	196.0	213.7	218.3	220.3	223.0	229.0	233.0
	(v/v)	± 3.1	± 2.5*	± 4.7*	± 5.8*	± 4.3*	± 4.6*	± 4.5*	± 5.0*
5	100 %	160.7	183.7	200.3	203.7	203.7	208.3	209.3	214.7
	(v/v)	± 2.7	± 5.0*	± 5.2*	± 6.4*	± 6.4*	± 5.2*	± 4.7*	± 5.3*

Note: The results are mean ± SEM for n=3; * Statistical significance ($p < 0.05$) as compared to the initial body weight.

Table 2: Results on glucose level, liver and kidney functions of rats after administration of honey

Group	Treatment	Glucose (mg/dL)	Urea (mg/dL)	Creatinine (mg/dL)	ALP (U/L)	ALT (U/L)
1	distilled	118.0	25.7	0.25	262.3	73.0
	water	± 14.7	± 3.8	± 0.02	± 17.1^{d}	± 9.9^{d}
2	10 %	117.7	22.7	0.22	238.5	59.3
	(v/v)	± 11.6	± 2.6	± 0.02	± 0.5^{d}	± 2.0^{d,e}
3	20 %	127.7	24.7	**0.30**	243.3	70.7
	(v/v)	± 1.7	± 1.8	**± 0.04^{e}**	± 9.6^{d}	± 3.9^{d}
4	50 %	141.3	23.0	0.23	340.3	98.7
	(v/v)	± 1.9	± 2.5	± 0.03	± 12.8^{a,b,c,e}	± 2.8^{a,b,c}
5	100 %	122.0	23.0	**0.16**	**273.7**	**86.7**
	(v/v)	± 3.6	± 1.2	**± 0.06^{c}**	**± 12.8^{d}**	**± 10.9^{b}**

Note: The results are mean ± SEM for n=3; ALP: alkaline phosphatase; ALT: alanine aminotransferase. a= statistical significant ($p < 0.05$) as compared to group 1, b= statistical significant ($p < 0.05$) as compared to group 2, c = statistical significant ($p < 0.05$) as compared to group 3, d = statistical significant ($p < 0.05$) as compared to group 4, e = statistical significant ($p < 0.05$) as compared to group 5.

4. Discussion

The main uses of honey are in cooking, baking, as a spread on bread, and as an addition to various beverages, such as tea, and as a sweetener in some commercial beverages. It consists of primarily sugars such as monosaccharides, disaccharides, oligosaccharides and polysaccharides (Bogdanov *et al.*, 2008; Erejuwa *et al.*, 2012). It contains enzymes such as glucose oxidase, diastase, invertase, catalase and peroxidase (Bogdanov *et al.*, 2008). Honey also contains other bioactive constituents such as organic acids, ascorbic acid, trace elements, vitamins, amino acids, proteins and Maillard reaction products (Bogdanov *et al.*, 2008). Being rich in carbohydrates like glucose and fructose when ingested could be metabolized to generate energy and help in tissue repair. This paper reports the effect of honey on heamatological and biochemical parameters at various concentrations in normal albino rats.

Table 3: Results of plasma protein level of rats after administration of honey

Group	Treatment	Total protein (g/L)	Albumin (g/L)	Globulin (g/L)	A/G ratio
1	distilled water	7.4 ± 0.4	3.1 ± 0.1	4.2 ± 0.5	0.8 ± 0.1
2	10 % (v/v)	7.6 ± 0.6	3.2 ± 0.2	4.4 ± 0.5	0.7 ± 0.1
3	20 % (v/v)	7.9 ± 0.3	3.3 ± 0.1	4.7 ± 0.4	0.7 ± 0.1
4	50 % (v/v)	7.3 ± 0.1	3.3 ± 0.1	4.1 ± 0.1	0.8 ± 0.0
5	100 % (v/v)	6.5 ± 0.9	3.1 ± 0.1	3.3 ± 0.9	1.2 ± 0.4

Note: The results are mean ± SEM for n=3; A: albumin; G: globulin. a= statistical significant ($p < 0.05$) as compared to group 1, b = statistical significant ($p < 0.05$) as compared to group 2, c = statistical significant ($p < 0.05$) as compared to group 3, d = statistical significant ($p < 0.05$) as compared to group 4, e = statistical significant ($p < 0.05$) as compared to group 5.

Table 4: Results of lipid profile of rats after administration of Honey

Group	Treatment	Cholesterol HDL ratio	Cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
1	distilled water	1.4 ± 0.0	60.7 ± 6.7	89.3 ± 13.7	43.3 ± 3.8	16.0 ± 1.5	17.7 ± 2.8
2	10 % (v/v)	1.6 ± 0.0	68.0 ± 3.5	**119.0 ± 11.0^{d,e}**	44.0 ± 3.2	20.7 ± 2.3	**23.3 ± 2.0^{d,e}**
3	20 % (v/v)	1.5 ± 0.1	62.3 ± 3.2	87.0 ± 8.5	42.7 ± 0.9	19.7 ± 2.7	17.3 ± 1.7
4	50 % (v/v)	1.5 ± 0.1	62.3 ± 3.2	74.7 ± 17.4^{b}	40.0 ± 4.4	19.3 ± 2.9	14.3 ± 3.3^{b}
5	100 % (v/v)	1.4 ± 0.1	55.0 ± 2.9	**60.3 ± 4.3^{b}**	39.0 ± 1.2	17.0 ± 1.7	**11.7 ± 0.9^{b}**

Note: The results are mean ± SE for n=3; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein. a = statistical significant ($p < 0.05$) as compared to group 1, b= statistical significant ($p < 0.05$) as compared to group 2, c= statistical significant ($p < 0.05$) as compared to group 3, d= statistical significant ($p < 0.05$) as compared to group 4, e= statistical significant ($p < 0.05$) as compared to group 5.

Our study indicates an increase in body weight among all the experimental animals as the administration progressed from day 1 to day 7. Within the same treatment groups, there was an increase from 10% to 20% (v/v) but this was observed to start decreasing as the concentration increased. The observed increase in body weight could be due to the androgenic properties of the honey since androgens possess anabolic activity (Johnson *et al.*, 1988). Moreover, decrease in body as a result of increased in concentration might be because of the fact that honey triggers a small spike in insulin levels (the glucose in honey stimulates in a small insulin release), and insulin stimulates the release of tryptophan in the brain. Tryptophan is converted to serotonin, which in the dark is converted to melatonin. Melatonin in return inhibits the release of insulin, thus further stabilizing blood sugar levels during the night (Ron, 2007) and this by implication down regulate the aerobic glycolytic pathway that is believed to play a vital role in lipogenesis which will ultimately lead to an increase in body weight.

Table 5: Results on Hematological parameters of rats after administration of honey

Group	Treatment	Hb (g/dL)	RBC (million /µL)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/dL)	WBC ($\times10^9$/L)	PLT ($\times10^9$/L)
1	Distilled	11.9	6.4	35.1	55.1	18.6	33.8	4.1	914
	water	± 0.1	± 0.1	± 0.6	± 0.6	± 0.3[b,c]	± 0.6[e]	± 1.4[c]	± 19.5
2	10 %	12.1	6.2	34.5	60.7	19.6	34.1	3.3	555.0
	(v/v)	± 1.9	± 0.9	± 4.5	± 1.7	± 0.1[a]	± 0.9	± 1.7[c]	± 0.0[e]
3	20 %	**13.1**	**6.6**	**37.6**	57.3	**19.9**	34.8	**8.5**	661.0
	(v/v)	**± 0.5**	**± 0.2**	**± 1.6[d,e]**	± 0.4[e]	**± 0.3[a,e]**	± 0.3	**± 0.7[a,b,e]**	± 0.0[e]
4	50 %	11.7	5.6	30.8	55.3	19.4	35.1	6.2	850.0
	(v/v)	± 0.8	± 0.2	± 1.6[c]	± 0.7	± 0.3	± 0.1	± 0.6e	± 0.0
5	100 %	11.0	5.8	30.5	53.5	19.0	35.6	2.3	**991.0**
	(v/v)	± 0.0	± 0.1	± 0.4[c]	± 0.2[c]	± 0.2[c]	±0.5[a]	± 0.2[c,d]	**± 0.0[b,c]**

Note: The results are mean ± SEM for n=3; Hb: hemoglobin; RBC: red blood cell count; PCV: packed cell volume; MCV: mean cell volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; WBC: white blood cell count; PLT: platelet. a = statistical significant ($p < 0.05$) as compared to group 1, b = statistical significant ($p < 0.05$) as compared to group 2, c = statistical significant ($p < 0.05$) as compared to group 3, d = statistical significant ($p < 0.05$) as compared to group 4, e = statistical significant ($p < 0.05$) as compared to group 5.

The observed decrease in the level of creatinine, ALP and ALT activities is a clear vindication that the honey is having hepatoprotective and renal protective properties and this is in accordance with the fact that consumption of honey conferred the aforementioned effects (Wilson *et al.*, 2011). There were also no effects on cholesterol, HDL, LDL and cholesterol HDL ratio. However, the observed decreased level of triglyceride and VLDL indicates the fact that the treatments might not be having lipogenic effects. This further confirms why there was a decreased in body weight as the concentration increased.

Honey administration tends to have stabilizing effects as there were no effects on total protein, albumin, globulin and albumin/globulin ratio as well as hemoglobin, red blood cell counts. Furthermore, an increased in packed cell volume, mean corpuscular hemoglobin and white blood cell counts at 20% (v/v) treated group corroborate the honey as an anti-anemic and immune-stimulant agent (Fiorani *et al.*, 2006). There were also increased in platelet and decreased in mean cell volume and mean corpuscular hemoglobin concentration in a concentration dependent manner. This is in accordance of the fact that exclusive honey feeding significantly modifies the hematological parameters (Noori *et al.*, 2006).

5. Conclusion

The results from this study indicate that daily consumption of honey might have some positive and negative effects on body weight, biochemical and hematological parameters on consumers depending on the concentration.

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