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ORIGINAL ARTICLE

Hepatoprotective Role of Propolis Extract to Prevent Hepatotoxic Effects of ATT in patients with Tuberculosis

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ABSTRACT

Objective: The main purpose of this study is to evaluate the hepatoprotective effects of propolis in hepatocytes injury caused by ATT due to isoniazid and rifampicin.

Methods: Healthy albino rats of with average weight of 200-250g were under this study. These rats dividing into main four groups, A group is taken a control group and then further into the group B, group C, and group D as group for experiments. The control group had 15 rats with measured weight, they were given distilled water. Group B had 15 rats, they were given with standard dose of rifampicin and isoniazid. Group c had 15 rats, they were also given with standard dose of rifampicin and isoniazid. Group D had 15 rats, they were given with standard dose of rifampicin and isoniazid and also extract of the propolis we prepared.

Results: Serum ALT in the experimental group B with group C, group D were also found to be of statistically significant with p-value < 0.001. ALT serum level observed high in group B. Multiple comparison between groups revealed that group B with a significantly increase in the serum enzyme AST level in comparison to group A, group C and group D with p-value <0.001.

Conclusion: This study showed that ethanolic extract of propolis prevents isoniazid and rifampicin induced hepatotoxicity in the albino rats.

Key words; Propolis, Anti-tuberculosis treatment, Hepato-toxicity.

INTRODUCTION

Propolis is a natural occurring product which is derived from the plant resins and it is collected by the one type of Bee called Apis mellifera bee. Propolis is used widely for different infections and wound healing because of it having many chemical substances and enzymatic properties. It also has antimicrobial anti-inflammatory, anti-viral bacteriolysis activity and inhibit bacterial protein synthesis.[1,2] Propolis havening many chemical compounds and is biological activity including its anti-inflammatory benefits it is also used to reduce side effect of ATT in tuberculosis. Tuberculosis is a disease caused by Mycobacterium Tuberculosis. This disease is infecting mainly lungs and also bones, lymph node, meninges, GIT and genitourinary system.[3,4] The first line therapy given is from six to nine month with isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin. Second line of drug kanamycin, ofloxacin, cyclomerize and ciprofloxacin. These drugs also have side effects on different body organs especially liver. During ATT liver enzyme level is monitored during therapy. There are derange level liver biomarker and abnormal rise of ALT, AST.[5-7]

Isoniazid is first line of drug used in ATT. In the liver isoniazid is firstly metabolized by enzymes of liver and its byproducts are the main source which leads to damage the hepatic cells. Liver cytochrome system is a fighting source against this damage.[8,9]

Rifampicin a drug of ATT is a semisynthetic derivative of the rifamycin. This gives orange color to tears and urine include rash thrombocytopenia, nephritis and abdominal discomfort. Mainly hepatotoxic effects are contributed by CYP2E1 is involved in isoniazid related hepatotoxicity. It also elevates the level of IL-8 and NO.[10,11]

MATERIAL AND METHODS

Healthy albino rats of with average weight of 200-250g were under this study. These rats dividing into main four groups, A group is taken a control group and then further into the group B, group C, and group D as group for experiments. The crud form of propolis obtained from hives and prepared ethanol extracts using 100 grams with 95% ethanol. The dried form obtained by using dry rotatory evaporator method. To analyzed the data the tool used is SPSS 20.0 and by mean standard deviation +S. D and also to compare the difference between groups ANOVA is uses

Control group A;

This control group had 15 rats with measured weight. They were given distilled water.

Experimental one group B;

In this experimental group there are also 15 rats with measured weight. They were given with standard dose od rifampicin and isoniazid.

Experimental two group C;

This group also had 15 rats their weights are also noted. They were also given with standard dose of rifampicin and isoniazid.

Experimental three group D;

This group also have 15 rats their weights are also noted. They were given with standard dose of rifampicin and isoniazid and also extract of the propolis we prepared.

RESULTS

Serum Level of Alanine Amino Transferase (ALT); There the level of Comparison in the level of serum ALT in the experimental group B with group C, group D were also found to be of statistically significant with p-value < 0.001. ALT serum level observed high in group B.

Serum Level Aspartate Amino Transferase (AST): Multiple comparison between groups revealed that group B with a significantly increase in the serum enzyme AST level in comparison to group A, group C and group D with p-value <0.001. Comparison of the serum enzyme AST level experimental group B with C and D was found to be of statistically significant with p-value 0.001.

Table 1. Serum Level of ALT

groups	Serum level of ALT before the mean	Serum ALT before the standard deviation	Serum AST before mean	Serum AST after standard deviation
GROUP A	28.2	3.0	30.1	2.7
GROUP B	27.1	2.5	64.4	3.6
GROUP C	25.6	2.8	51.2	2.5
GROUP D	26.4	2.6	44.5	3.6

Table 2. Comparison of Serum Alt Levels for Four Groups with One Way ANOVA.

		Sum of all square	df	Mean square	f	P value
BEFORE	BETWEEN GROUP	60.6	3	20.19	2.51	0.068
	WITHNIN GROUP	450.0	56	8.04		
	TOTAL	510.6	59			
AFTER	BETWEEN GROUP	9250.3	3	3083	296.55	<0.001
	WITHIN GROUP	582.3	56	10.40		
	TOTAL	9832.6	59			

Table 3. Serum AST Levels in Animals at The and End of Experiment for Four Groups

Group	AST serum level			
	Before		after	
	Mean	SD	mean	SD
Group A	126.4	4.6	127.07	4.18
Group B	126.9	5.5	269.13	6.51
Group C	128.1	3.7	174.13	5.78
Group D	127.3	4.0	122.87	4.66

Table 4. Comparison of AST Levels for Animals Before and After in Four Groups with Help of One-Way ANOVA

		Sum of all squares	df	Mean square	f	P value
before	Between the groups	21.8	3.0	7.30	0.35	0.781++
	Within all groups	1138.3	55	20.32		
	Total	1160.2	58			
After	Between the groups	207986.4	3.0	69328.81	2411.24	< 0.001*
	Within the groups	1610.0	565	28.74		
	Total	209596.5	58			

DISCUSSION

Mycobacterium Tuberculosis (TB) is one of the effecting disease and ATT used have other health effects. Drugs included isoniazid (INH), rifampicin (RIF), Pyrazinamide (PZA) and ethambutol. These ATT are common hepatotoxic agents. In our study, ethanolic extract of propolis might be responsible to keep the enzymes near normal. In groups C and D in which ethanolic extract of propolis was given for 30 days, these were significantly less to the extent that these almost resemble the level of those of the control group A. It could be postulated that the hepatoprotective effect of propolis ethanolic extract was, due to its ability to inhibit membrane lipid per oxidation and free radical formation on account of their free radical scavenging ability.[2,3,7,8]

This study showed that ethanolic extract of propolis prevents isoniazid and rifampicin induced hepatotoxicity in the albino rats. Propolis extracts given to the rats has shown positive effects to control the side effects of isoniazid and rifampicin causing hepatotoxic effect, in clinical biochemically. It is worth noting that isoniazid and rifampicin metabolized in the liver and due to its complete metabolism in hepatocytes caused hepatotoxicity. The hepatoprotective role of propolis is mainly effective due role of its antioxidant components. Other detailed studies are much needed to see the better and other protective role of propolis on hepatocytes due to damage caused by isoniazid and rifampicin induced liver damage in human beings.

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