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STUDIES ON MEDICINAL HERBS-I: SERUM BIOCHEMICAL CHANGES INDUCED IN RABBITS BY ADMINISTRATION OF *COLCHICUM AUTUMNALE*

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Powdered roots of *Calchicum autumnale* and pure colchicin were administered orally to rabbits at a dose of 1.5 mg/kg and 0.25 mg/kg respectively. Five doses were administered at 0,24,48,72 and 96 hours. The serum was analysed at 6,12,24,48,96, 144 and 192 hours after the last dose. Both drugs induced a decrease in serum cholesterol and uric acid, while an increase in lipids was observed. Although the lipids became normal at the end of the experiment, the values of cholesterol and uric acid were still different ($p<0.01$) from the control. The glucose did not give a defineable pattern. The activity of serum LDH was increased by the crude drug and decreased by pure colchicine. Activities of SGOT and SGPT were decreased significantly by the crude drug.

Key words: Medicinal herbs, Serum, Rabbits

Introduction

Colchicine ($C_{22}H_{25}NO_6$) is a unique anti-inflammatory alkaloid [1]. The total amount of alkaloids in *Colchicum autumnale* is 1.7%, being four times as high in the seeds as in other parts of the plant [2]. The effect of colchicine on various vital metabolic processes of rats, mice, pigs, rabbits, dogs and chicken have shown that colchinine inhibited the rate of uric acid. Synthesis [3,4]. Colchicine was found to be effective in preventing gouty inflammation in mice [5]. The formation of uric acid from xanthine is catalysed by the action of xanthine hydrogenase, it has been observed that colchicine is a powerful inhibitor of hepatic xanthine dehydrogenase in pigs and chicken liver [6]. Rubulis *et. al.* [7] found that colchicine decreased the fecal bile acid and sterol excretion. Hadnagy *et. al.* [8] have reported that colchicine inhibited (10-43%) glucose uptake in dogs. Colchicine and some of its derivatives possess antitumour activity [9]. The purpose of this study was to observe the biochemical changes induced by powdered *Colchicum autumnale* on serum of rabbit and to compare these with the pure colchicine.

Materials and Methods

Animals used. Fifteen adult male rabbits *Oryctolagus cuniculus* weighing 0.82-1.15 kg were used. The animals were kept in the animal house of the Department of Pharmacy and exposed to natural photoperiod and temperature. The experiments were performed in June-July and during this period the temperature was 35-40.5° and humidity 24 to 98%. During the acclimatization period of 72 hours, water and fresh green fodder (clover) was provided *ad. Libitum.*

Procedure. Animals were divided into three groups of five animals each. One group was labelled as a control, while the other two groups were experimental. Powdered roots of *Colchicum autumnale* (1.5 mg/kg body weight) and pure colchicine (0.25 mg/kg body weight) were filled in the gelatin capsule and were administered orally to the respective group of experimental animals after every 24 hours for five consecutive days.

Collection of blood. The blood sampling was carried out after the last dose (a total of 5 capsules containing a cumulative dose of 7.5 mg of crude and 1.25 mg of pure drug) of the drug at the intervals of 6,12,24,48,96, 144 and 192 hours. The blood samples were obtained from the ear vein and allowed to clot in the refrigerator. The serum was separated by centrifugation at 4500 rpm.

Biochemical analyses. Blood serum was analysed to estimate uric acid, cholesterol, total lipid and glucose. The serum was also analysed to determine the activities of lactate dehydrogenase [10], serum aspartate transaminase and alanine transaminase [11].

Results and Discussion

Powdered roots of *Colchicum autumnale* (1.5 mg/kg body weight) and pure colchicine (0.25 mg/kg body weight) were administered after every 24 hours for five consecutive days during that period no mortality or change in weight of rabbits was observed.

An acute decrease in serum uric acid was observed with both the drugs and it was found that pure Colchicine decreased the uric acid more than the crude form. The values remained low for 24 hours but became comparble to the control at 48 hours. The values remained almost the same till 96 hours after which time a trend towards increase was seen in the pure colchicine treated rabbits and the values became siginificant at 144 hours. At this stage the crude drug treated rabbits had

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values slightly lower than the controls. The uric acid then increased and at the end of the experiment the serum uric acid was significantly ($P<0.01$) higher than the controls (Fig. 1). There are reports in the literature which shows that pure colchicine decreases the activity of two important enzymes namely xanthine oxidase and xanthine dehydrogenase which are important in the synthesis of uric acid in the body [12]. The

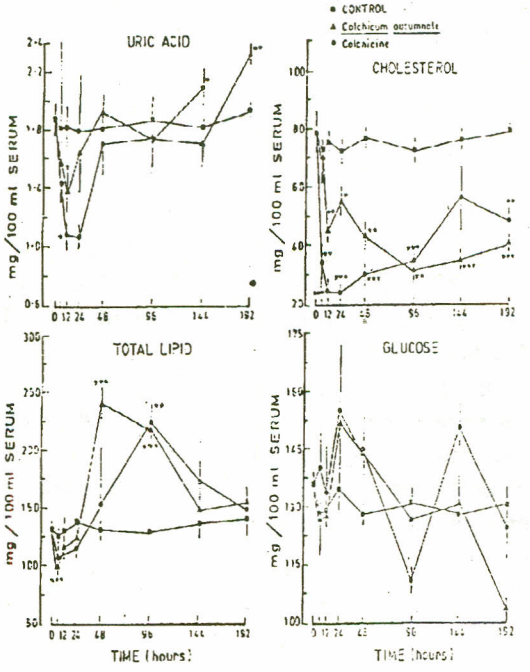

Fig 1. Effect of *Colchicumautumale* (1.5 mg/kg body weight) and pure-Colchicine (0.25 mg/kg body weight) (-0-) on serum uric acid, cholestrol, total lipid and glucose of adult rabbits, after oral administration for five consecutive days.

increasee in the values of serum uric acid at the end of the experiment can be due to wearing off the effect of drug on the enzyme systems reported above and the enzyme showing a rebound effect or the uric acid was being accumulated in the serum because of the impairment of the renal function [13].

Both crude and pure colchicine induced an acute hypocholesteremia which was more pronounced in pure colchicine treated rabbits. The hypocholesterimic condition persisted throughout the experimental period (Fig 1). This decrease in serum cholesterol in colchicine treated rabbits can be due to many reasons. The exact mechanism of action of colchicine is unknown at present. But it appears that probably liver function has been altered and the synthesis of hepatic cholesterol was inhibited. It is also possible that excessive synthesis of bile occured causing are distribution of cholesterol in the body [14]. This decrease in cholesterol is also interesting when the increase in total serum lipids is taken into account.

A decrease of lipids was observed in both crude and pure drug treated rabbits after 6 hours and then the serum lipid started increasing, it was maximum at 48 and 96 hours in animals treated with crude and pure drug respectively. The values then kept on subsiding and at the end of experiment the concentration of lipid was similar to the control values (Fig. 1). Rosenbloom *et. al.* [15] has reported the transitory induction of hyperlipidemia by pure colchicin. It is remarkably important to note the early onset of lipemia in crude drug treated rabbits and this increase might be induced by some other constituents present in the crude drug.

The zero hour values for glucose (n=15) were 137.41±2.94 mg/100 ml. The serum glucose fluctuated during 96 hours and at this time the values were little lower than the control values. After this the glucose first increased and then decreased again exhibiting a non-definable pattern and it is difficult to explain whether this was due to drug or a manifestation of the stress (Fig. 1).

The effects of crude drug on some serum enzymes which are indicative of hepatic function were also studied. The crude

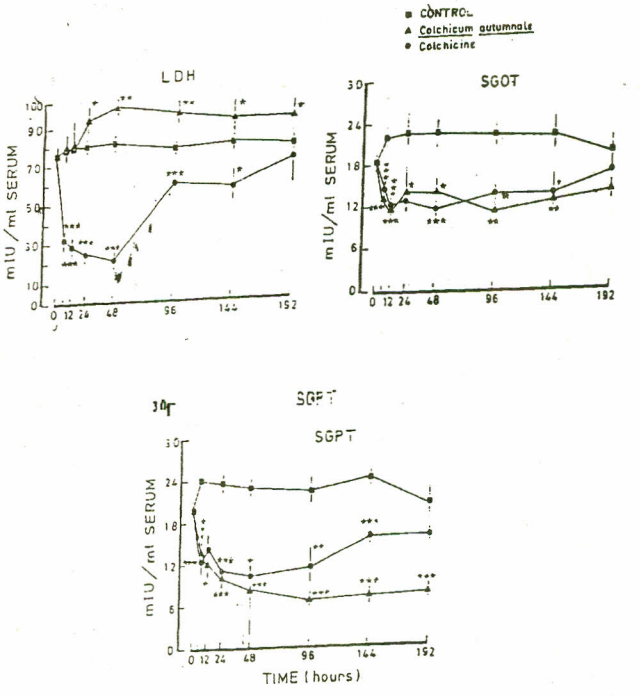

Fig 2. Effect of *Colchicum autumale* (1.5 mg/kg body weight) (--) and pure Colchicin (0.25 mg/kg body weight (-0-) on serum LDH, SGOT and SGPT activities of adult rabbits, after oral administration for five consecutive days.

drug showed an increase in the LDH activity of the enzyme after 24 hours and this increase in activity remained elevated till the end of the experimental period. In pure drug treated animals the LDH activity exhibited a significant decline even after 6 hours. The maximum decline in activity was observed at 48 hours and then it started increasing and at the end of the stipulated period the values were comparable to the control values (Fig. 2).

The two transaminases (SGOT and SGPT) were also studied, both crude and pure drug decreased the activity of these enzymes. The crude drug had a slightly stronger response than the pure drug. The activity in pure colchicine treated rabbits became similar to the controls at the end of the experiment, but in crude drug treated animals, the activities of the enzymes were still lower than the controls. (Fig. 2) These changes in the transaminases were due to the fact that both drugs effect the amino acid and protein metabolism [14]. From the above discussion it may be concluded that both the drugs induced a decrease in serum cholesterol and uric acid. The crude drug increased the activity of serum LDH and significantly decreased the activities of SGOT and SGPT.

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