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Effect of administration of apple juice on brewer's yeast-induced pyres is in rats

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Abstract
Background: Apples are rich source of phytochemicals, and their consumption linked with reduced risk of some cancers, cardiovascular disease, asthma, and diabetes. In the laboratory, apples have been found to have very strong antioxidant, inhibit cancer cell proliferation, decrease lipid oxidation, and lower cholesterol.
Objective: Evaluation of the antipyretic effect of apple juice.
Methods/ Design: Twenty albino rats were used in the study. Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension, and the rectal temperature of each rat was measured, before and after 17h of injection of the yeast, and every hour for four hours after treatment. The rats were divided into: group A as control, Group B treated with paracetamol, group C treated with apple juice.
Results: The results showed no significant changes in rectal temperature in group A after 1, 2, 3, and 4hour from the initial time, while demonstrated a significant decrease in group B after 1 and 2 hour of treatment, and significant decrease in group C after 1, 2, 3 and 4 hour of treatment, and when the rectal temperature after 1h, 2h, 3h, and 4h in groups B and C were compared to their relatives In group A, there was a significant decrease in group B after 1 and 2 hour of treatment, while a significant decrease after 1, 2, 3 and 4 hour in group C.
Conclusion: Apple is effective as antipyretic. However, describing the active constituent which is responsible for antipyretic effect and its mechanisms of action are required.

Keywords: apple juice, brewer's, yeast-induced

1. Introduction
Fever is defined as the elevation of core body temperature above normal [1]. Pyres is a clinical condition that results in increase in body temperature. Pyrexia or fever arises as a secondary impact of infection, malignancy or other diseased state [2]. Normally the infected or damaged tissue initiates the enhanced formation of proinflammatory mediator's which increase the synthesis of prostaglandin E2 near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature [3]. Evidence suggests that cytokines produced peripherally or centrally are involved directly in the complex autonomic febrile response. In the periphery, IL-1 and TNF induce an increased production of IL-6. Large amounts of IL-6 have been found to be present in all febrile diseases [4]. Apples contain a large concentration of flavonoids, as well as a variety of other phytochemicals that have been found to have very strong antioxidant activity, inhibit cancer cell proliferation, decrease lipid oxidation, and lower cholesterol, and also led to a decrease in LDL oxidation in human serum [5, 6].
In addition to that, atherosclerotic lesions in mouse blood vessels were reduced by up to 38% following dietary supplementation with apple extracts rich in polyphenols [7], and when pure extracts of the dietary flavonoids quercetin or epicatechin (both common to apples) were given to healthy men, an improvement in endothelial function was observed [8]. The compounds most commonly found in apple peels consist of the procyanidins, catechin, epicatechin, chlorogenic acid, phloridzin, and the quercetin conjugates. In the apple flesh, there is some catechin, procyanidin, epicatechin, and phloridzin, but these compounds are found in much lower concentrations than in the peels. The procyanidins, epicatechin and catechin, have strong antioxidant activity and have been found to inhibit low density lipoprotein (LDL) oxidation in vitro [10].
Recently, apples have been put to the test with a more biologically relevant method of assessing antioxidant [11]. Compared with 25 other fruits commonly consumed apples are the largest contributor of fruit phenolics and the greatest supplier of cellular antioxidant activity [12].

The total antioxidant activity of apples with the peel was approximately 83 µmol vitamin C equivalents, which means that the antioxidant activity of 100 g apples is equivalent to about 1500 mg of vitamin C. However, the amount of vitamin C in 100 g of apples is only about 5.7 mg [5].

Consumption of fresh fruit is often replaced by the intake of fruit juices, due to their convenience and ability to quench thirst. In Europe, apple juice is a highly-consumed product, in second place after orange juice. Some authors have suggested that apple juice can reduce some forms of cancer [13].

Search for safe herbal remedies with potent antipyretic activity received momentum recently as the available antipyretics, such as paracetamol, aspirin and nimusulide etc, which have toxic effect to the various organs of the body [14]. Flavonoids are known to target prostaglandins which are involved in the pyrexia. Hence the presence of flavonoids in the apple may contribute to antipyretic activity [15].

2. Materials and methods

2.1 Preparation of apple juice

Apple juice prepared freshly at the time of experiment by using juice blender that crushing and pressing apple pulp, without adding water or any other additives.

2.2 Animal

The study carried out in July 2014 in the department of pharmacology / college of medicine / Wassit University. The albino rats were randomly distributed into control and test groups. Twenty albino rats of both sex weighing 150 – 200g from the animal house of the college of Sciences / Wassit University, were used for the study. The animals were kept in clean and dry plastic cages, with 12h: 12h light dark cycle. The animals were fed with standard pellet diet and water was given ad libitum.

2.3 Antipyretic activity

Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension (10 ml/kg) into the animal's dorsum region (as described by Adams *et al*. 1968).

The rectal temperature of each rat was measured using a thermometer before injection of the yeast, at 17 h following yeast injection (to determine the pyretic response to yeast) and every hour for four hours after treatment.

The animals were then fasted for the 17 hour and water was provided ad libitum. Only rats that showed an increase in temperature of at least 0.5 °C were employed for the experiments. The apple juice and paracetamol (100 mg/kg) was administered orally and the temperature was measured at 0, 1, 2, 3 and 4 h after administration.

The rats were divided into three groups as following.

- **Group A (Control):** include five rats, no treatment was administered.
- **Group B:** include five rats treated with paracetamol (Julphar®, UAE) as positive control.
- **Group C:** include ten rats, treated with 3 ml of apple juice.

2.4 Statistical analysis

All data were expressed as mean ± S.D. and analyzed statistically by using Student's t-test and paired t-test. A difference was considered significant at $P<0.05$.

3. Results

The results of the antipyretic activity are presented in Table 1. Administration of the yeast to the rats produced significant increase in rectal temperature 17 hour after yeast injection and continued throughout the test, there was no significant difference (P- value > 0.05) in the basal temperature at initial time (0 hour) between the different groups.

The results demonstrated no significant (P- value > 0.05) changes in rectal temperature in group A (control) after 1, 2, 3, and 4hour from the initial time (0hour), but showed a significant decrease (P- value < 0.05) in mean rectal temperature in group B after 1and 2 hour of treatment with paracetamol (100mg/kg) when compared to initial temperature (after 17 hour from injection of brewer's yeast).

The results also showed a significant decrease (P- value < 0.05) in mean rectal temperature in group C after 1, 2, 3 and 4 hour of treatment with 3ml of apple juice when compared to initial temperature (after 17 hour from injection of brewer's yeast).

In addition to that, when the rectal temperature after 1h, 2h, 3h, and 4h in groups B and C were compared to their relative rectal temperature in group A (where no treatment was administered), there was significant (p- value < 0.05) decrease after 1h, 2h, 3h, and 4h in group B, and only after 1h and 2h in groups B, without significant (P- value > 0.05) differences in rectal temperature after 3 and 4 hour of treatment.

Table 1: Effects of the Apple juice on brewer's yeast-induced pyrexia in rats.

Groups	dose	Rectal temperature (°C)		Temperature after treatment (°C)			
		Normal	(initial temp) After yeast + 17 h	+1h	+2h	+3h	+4h
Group A (control)n5		38.48 ± 0.629	39.47± 0.531	39.85± 0.2646	40.27± 0.263	39.85 ± 0.3416	40.15± 0.4123
Group B n5 (paracetamol)	100mg/kg	38.62 ± 0.6535	39.3± 0.6892	38.24 [a] *± 0.7403	38.24[a] *0.7403	38.54± 1.167	39 ± 1.134
Group C (apple juice)n=10	3ml	38.35 ± 0.3923	39.31 ± 0.4067	37.75 [a]*± 0.7028	38.31 [a] * ± 0.6262	38.76 [a] * ± 0.4648	38.61 [a] * ± 0.7325

[a] P<O.O5 when compared to the relative control temp.

*P<O.O5 when compared to initial temp. (0h) within the same row.

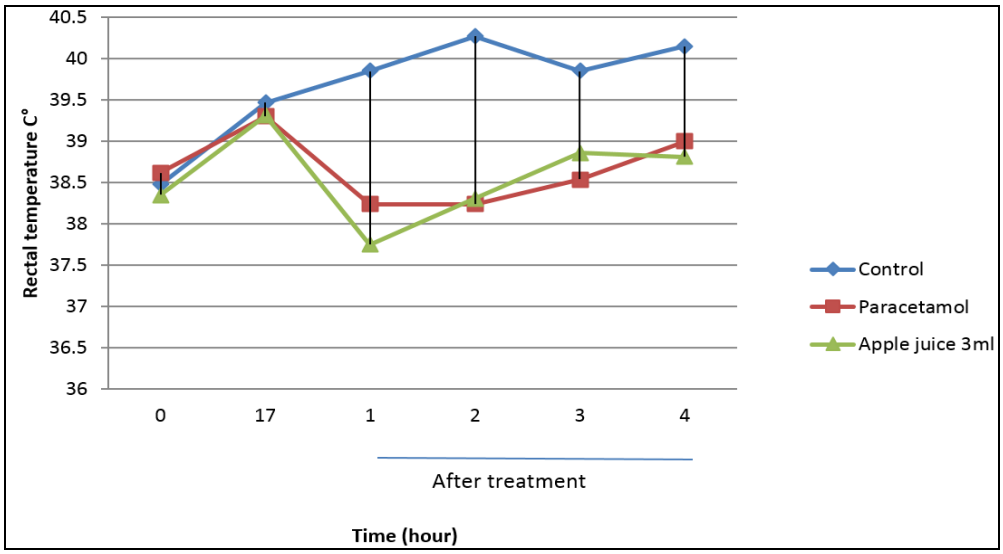

Fig 1: Effect of Apple juice in hyperpyretic rats

4. Discussion

Bacteria cause fever because of the endotoxin lipopolysaccharide found in their cell wall. The subsequent elaboration of interleukin-1 and tumour necrosis factor-α is believed to initiate the synthesis and release of the fever-causing autacoid prostaglandin E2 (PGE2) by the endothelium and pericytes of brain capillaries [16].

In general, non-steroidal anti-inflammatory drugs produce their antipyretic action through inhibition of prostaglandin synthetase within the hypothalamus [17]. The apple juice showed significant antipyretic activity in rats is due to the presence of the flavanoids, like for example quercetin, and catechin. Therefore it appears that antipyretic action of apple may be related to the inhibition of prostaglandin synthesis in hypothalamus, as some flavonoids are predominant inhibitors of cyclooxygenase or lipooxygenase [14]. The antipyretic effect of apple make the apple juice as a good substituent to other synthetic antipyretic, due to it is safety (no toxic effect), tolerability by the patients, in addition to other beneficial effects like the antioxidant and cardiovascular protective effects. Ray *et al*., (2006) evaluate the antipyretic effect of ethyl acetate extract of Acacia catechu Willd in albino rats and the results showed there was a significant antipyretic effect, Catechu or cutch (Katha in Hindi and Manipuri), contains catechuic acid, catechutannic acid, acacatechin, catechu red, quercetin, catechin, epicatechin, phlebotanin, gummy matter, quercitrin, and epicatechin [18]. Both the ethyl acetate extract of Acacia catechu Willd and apple juice have significant antipyretic effect, and the presence of the catechin, epicatechin and quercetin in the composition of Acacia catechu Willd and apple juice may be responsible for antipyretic properties of apple and catechu wild.

5. Conclusion

The results of the present study indicate the antipyretic activity of the apple juice is comparable to that of paracetamol and has significant priority to it. However, further investigations are required to know exactly the active constituents responsible for antipyretic effect and if oxidative stress involved in the pathogenesis of fever since apple has a potent antioxidant affect.

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