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# ANTI-INFLAMMATORY ACTIVITY OF SODIUM PYRUVATE – A PHYSIOLOGICAL ANTIOXIDANT

S. K. GUPTA*, S. RASTOGI[1], JAI PRAKASH, SUJATA JOSHI, Y. K. GUPTA, LEN AWOR AND S. D. VERMA[2]

*Department of Pharmacology,*
*All India Institute of Medical Sciences*
*Ansari Nagar, New Delhi – 110 029,*

[1]*Department of Orthopaedics,*
*All India Institute of Medical Sciences,*
*Ansari Nagar, New Delhi – 110 029*

*and*

[2]*Department of Ophthalmology,*
*University of Maryland School of Medicine,*
*10S, Pine Street, Baltimore, Maryland – 21201*

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**Abstract :** The anti-inflammatory activity of sodium pyruvate was evaluated in acute and chronic models of inflammation in rats. Oral administration of sodium pyruvate at three different dose levels of 125, 250 and 500 mg/kg body weight significantly inhibited the carrageenan induced acute paw edema in a dose dependent manner. The effect of 500 mg/kg sodium pyruvate was comparable to that of 12.5 mg/kg of standard diclofence. In Freund's adjuvant arthritis model, oral administration of sodium pyruvate at the submaximal dose of 250 mg/kg once daily upto one week before Freund's adjuvant injection and immediately by the same route on the 7$^{th}$ day of adjuvant injection significantly reduced the edema at 18 hours after the challenge. The treatment was continued for 14 days thereafter in two divided doses of 125 mg/kg in the morning and 125 mg/kg in the evening. Sodium pyruvate showed significant anti-inflammatory activity at the 14$^{th}$ day (chronic phase) also. To conclude, sodium pyruvate exhibited significant anti-inflammatory activity in both the models of inflammation which could be attributed to its antioxidant properties.

**Key words :** sodium pyruvate carrageenan Friend's adjuvant paw edema antinflammatory

*Corresponding Author

## INTRODUCTION

Tissue injury caused by introduction of a foreign antigen, trauma or local exposure to certain chemicals triggers a complex process of inflammation. This may consist of a fluid stasis as well as accumulation of several cellular and non-cellular elements of the immune response. The prominent cellular elements invading the injury sites are lymphocytes, monocytes, macrophages and the various granulocytes (1). While all these elements are essentially immunoprotective in nature, simultaneous tissue injury also takes place. The injury is very frequently reflected by tissue degeneration and edema.

In this communication, we have studied the anti-inflammatory activity of sodium pyruvate. This substance being an α-keto acid, is rapidly decarboxylated producing acetic acid, carbon dioxide and water with the consequence of peroxide elimination from the mileu. This substance works as a peroxide scavenger (2). This would also result in the prevention of OH generation by the metal catalysed Fenton reaction. In a recent communication it has been shown to be an effective scavenger of superoxide also(3,4). Hence it scavenges most of the active species of oxygen. Its anti-inflammatory action has been tested in carrageenan and Freund's adjuvant induce paw edema in rats.

## METHODS

Sodium pyruvate, Carrageenan (TypeI, Cat No C-1013) and Freund's complete adjuvant were purchased from Sigma Chemicals Co., USA. Diclofenac sodium was generously gifted by Cipla Limited, Bombay. Young Wistar albino rats of either sex weighing 150-200 g were obtained from the Experimental Animal Facility of All India Institute of Medical Sciences and maintained under standard laboratory conditions of food and water. Indigenously made plethysmograph filled with mercury was used to measure the rat paw volume before and after the pyruvate treatment.

### Carrageenan induced acute rat paw edema

Anti-inflammatory activity of sodium pyruvate was measured according to the method of Winter et al (5). Rats were distributed into 5 groups consisting of 6 rats per group. Right hind paw edema was induced by subplanter injection of 0.1 ml of 1% carrageenan in normal saline. Sodium pyruvate was administered orally at three different doses of 125, 250 and 500 mg/kg body weight everyday, starting one week prior to carrageenan insult and simultaneously on day 7 by the same route (i.e. on the day of carrageenan injection) to the rats in individual group. To the positive control group diclofenac sodium was administered just in a single dose of 12.5 mg/kg immediately after carrageenan injection. Paw volume upto the ankle joint was measured using the graduated plethysmograph filled with mercury before and 3 hours after carrageenan challenge in each group.

### Freund's adjuvant induced rat paw edema

The method as described by Goel et al, 1990 was used with slight modification (6). Rats were distributed into 3 groups consisting of 6 rats per group. Edema (acute and chronic) was produced by subcutaneous injection of 0.1 ml of Freund's complete adjuvant into the right hind foot pad. Sodium pyruvate was fed orally at the

dose level of 250 mg/kg body weight to the treatment group, before injecting Freund's adjuvant (one week pretreatment). Treatment with sodium pyruvate was continued in two divided doses (one dose in the morning and one dose in the evening) for 14 days thereafter. Paw volume after 18 hours of adjuvant injection was taken as subacute phase of inflammation, while paw volume on the 14th day was taken as an index of chronic inflammation.

### Statistical analysis

The data was analysed using Student's unpaired t-test. The P value of <0.05 was considered significant.

## RESULTS

The results of studies conducted with sodium pyruvate are shown in Table I and Table II. In carrageenan induced model of inflammation sodium pyruvate inhibited the edema in a dose dependent manner. It was observed that 125, 250 and 500 mg/kg pyruvate inhibited the edema by 26.96% (P< 0.001), 39.76% (P<0.01) and 74.06% (P<0.01) respectively. Pyruvate at the dose of 500 mg/kg showed edema inhibition comparable to standard declofenac. In Freund's adjuvant arthritis model, pyruvate (250 mg/kg) inhibited the edema by 28.97% (P<0.01) in subacute phase (18 hours) and 30.01% (P<0.01) in chronic phase (14 days) of inflammation respectively as compared to control.

TABLE I: Anti-inflammatory effect of sodium pyruvate against carrageenan induced paw edema in rats.

| *Group* | *Edema volume in ml (Mean ± SD)* |
|---|---|
| Control (Carrageenan alone) | 0.586±0.040 |
| Sodium pyruvate (125 mg/kg) | 0.428±.039 (26.96%)*** |
| Sodium pyruvate (250 mg/kg) | 0.353±0.031 (39.76%)*** |
| Sodium pyruvate (500 mg/kg) | 0.152±0.062 (74.06%)*** |
| Diclofenac (12.5 mg/kg) | 0.088±0.051 (84.98)*** |

Number of rats per group (n)=6, ***P<0.001 compared with control. Value in the parenthesis indicate % edema inhibition.

## DISCUSSION

Currently, the most widely used NSAIDs suffer from inherent side effects, the most important being the gastrointestinal irritation. For chronic diseases like osteoarthritis and rheumatoid arthritis, one has to depend on these drugs for life long. Therefore, there is a continuous search for an ideal anti-inflammatory drug which is safe and effective. Although these compounds have been suggested to act as inhibitors of prostaglandin synthetase, more recent studies suggest that the inflammatory tissue damage is due to the liberation of reactive oxygen species (ROS) from the phagocytes invading the inflammation sites (1, 7. 8).

TABLE II: Anti-inflammatory effect of sodium pyruvate against Freund's adjuvant induced Paw edema in rats.

| *Group* | *Edema volume in ml (mean ± SD)* | |
|---|---|---|
| | *(At 18 hours)* | *(At 14th day)* |
| Control (Freund's adjuvant alone) | 0.863±0.024 | 0.723±0.026 |
| Sodium pyruvate (250 mg/kg) | 0.613±0.029 (28.97%)** | 0.506±0.023 (30.01%)** |

No of rats per group (n)= 6, **P<0.01 compared with control. Values in the parenthesis indicate % edema inhibition.

Hence, the therapy based on ROS scavengers, alone or in combination with NSAIDs is considered more beneficial. Since pyruvate is an endogenously produced ROS scavenger, the primary objective of these investigations was to study its own anti-inflammatory activity. Preliminary studies described herein are in accordance with the proposed hypothesis. It was found significantly effective against carrageenan as well as Freund's adjuvant induced inflammation of the rat paw. The rats in the pyruvate treated group were visualized for the presence of duodenal and gastric ulcers to rule out the potential of pyruvate to produce gastrointestinal irritation. None of the rats showed the presence of ulcers. Mortality was also not observed in either of the models of inflammation. Therefore it is reasonable to assume that pyruvate being a physiological antioxidant, is well tolerated when fed to the rats either acutely or on chronic basis.

The antioxidant effect of this compound on exogenous administration has been found in a number of others oxyradical induced pathologies such as myocardial infarction, renal diseases and cataracts (9, 10, 11). The effectiveness of pyruvate, in this study, could be related to its action as stimulation of glycolysis and citric acid cycle. Further studies with this compound in other models of inflammation are desirable.

## REFERENCES


1. Conner EM, Grisham MB. Inflammation, free redicals and antioxidants. *Nutrition* 1996; 12(4): 274–277.
2. Herz H, Blake DR, Grootveld M. Multicomponents investigations of the hydrogen peroxide and hydroxyl radical scavenging antioxidant capacities of biofluids: the role of endogenous pyruvate and lactate. Relevance to inflammatory joint diseases. *Free Radic Res* 1997; 26(1): 19–35.
3. Borle AB, Stanko RT. Pyruvate reduces anoxic injury and free radical formation in perfused rat hepatocytes. Am J Physiol 1996; 270 (3Pt 1): G535–G540.
4. Cicalese L, Lee K, Schraut W, Watkins S, Borle A, Stanko R. Pyruvate prevents ischaemia reperfusion mucosal injury of rat small intestine. *Am J Surg* 1996; 171(1): 97–101.
5. Winter CA, Risley EA, Nuss GW. Carrageenan induced edema in hind paw of rats as an assay for anti-flammatory drugs. *Proc Soc Exp Biol Med* 1962; 111: 544–547.
6. Goel RK, Banerjee RS, Acharya SB. Antiulcerogenic and anti-inflammatory studies with shilajit. *J Ethnopharmacol* 1990; 29(1): 95–103.
7. Winrow VR, Winyard PG, Morris CJ, Blake DR. Free radicals in inflammation: second messengers and mediators of tissue destruction. *Br Med Bull* 1993; 49(3): 506–522.
8. Parke DV, Sapota A. Chemical toxicity and reactive species. *Int J Occup Med Environ Health* 1996; 9(4): 331–340.
9. Crestanello JA, Kamelgard J, Whitman GJ. The cumulative nature of pyruvate's dual mechanism for myocardial protection. *J Surg Res* 1995; 59(1): 1987; 204.
10. Salahuddin AK, Clarck EC, Nath KA. Hydrogen peroxide induced renal injury. A protective role for pyruvate *in vitro* and *in vivo*. *J Clin Invest* 1991; 88(6): 1886–1893.
11. Varma SD, Morris SM. Peroxide damage to the eye lens: in-vitro protection by pyruvate. *Free Radic Commun* 1988; 4(5): 283–290.