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SHORT COMMUNICATION

DELAYED MANIFESTATION OF ULTRA VIOLET RADIATION INDUCED ERYTHEMA IN GUINEA PIGS BY SODIUM PYRUVATE - A FREE RADICAL SCAVENGER

S. K. GUPTA*, LEN AWOR, S. RASTOGI[1], JAI PRAKASH, Y. K. GUPTA, S. D. VARMA[2] AND T. VELPANDIAN

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

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Abstract : Sodium pyruvate, a free radical scavenger was evaluated for anti-inflammatory activity using UV radiation induced dermal erythema on guinea pig and compared with that of standard naproxen. Oral as well as topical pyruvate exhibited significant activity against UV induced dermal erythema model and the activity was comparable to that of naproxen. In the other pharmacodynamic studies, such as the studies on rat blood pressure, isolated guinea pig ileum and rat uterus, it showed no effect on any of these. In conclusion, sodium pyruvate showed a significant protection in the UV induced dermal erythema in guinea pigs. It also showed good absorption in UV-B range and this property can be utilised to develop the sodium pyruvate as a sunscreening agent.

Key words: sodium pyruvate, erythema, ultra-violet, anti-inflammatory, sunscreen

INTRODUCTION

Pyruvate is an endogenous metabolite detectable in significant amount in various body tissues like liver, kidney and plasma etc. Millimolar concentrations of pyruvate in plasma, achieved by systemic administration have been reported to have no apparent adverse effects (1). In the present study, pyruvate was assessed for anti-inflammatory activity against ultra-violet (UV) induced erythema in guinea pigs. Naproxen was used as a standard drug to compare its activity.

METHODS

Naproxen was obtained from Searle, India. Albino guinea pigs (200–300 g) were used. Sodium pyruvate (Sigma, USA) as 5% w/w ointment was prepared as follows :

*Corresponding Author

Present Address :
[1] Department of Orthopaedics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi – 110 029
[2] Department of Ophthalmology, University of Maryland, Baltimore, USA.

emulsifying white wax, soft paraffin and liquid paraffin in the ratio of 3:5:2 were melted in a beaker with constant stirring at 70°C over a water bath. Sodium pyruvate was dissolved in distilled water separately. While cooling, sodium pyruvate dissolved in distilled water, was added slowly with constant stirring to make a uniform ointment.

UV-induced erythema in guinea pigs and drug testing studies : The guinea pigs were fasted overnight but provided water *ad libitum*. Before UV exposure their dorsal skin was shaved using depilatory cream. The animals were observed for a period of 30 minutes for signs of any skin irritation due to application of the cream. The animals were observed for a period of 30 minutes for signs of any skin irritation due to application of the cream. The UV (UV-B, 315–280 nm) exposure was accomplished by using a modified method of Gupta and Levy (2). Briefly, the cylindrical UV-B (15 watt) tube was fixed in a radiation proof tubing fitted with a centrally attached hollow cylinder of 5 cm length and 2 cm diameter through which radiation was delivered for a period of 1, 2, or 4 min. The UV exposure for 2 min was standardized and used throughout the experiment. The circular area (measuring 4 cm^2 on each flank) was exposed to UV for 2 min. Observations were made at 1, 2 and 4 hrs and the developed erythema was graded on intensity of redness on a scale of 0–2, as follows :

0 – no evidence of erythema

1 – definite erythema

2 – intense erythema. An average grading index of each group was calculated based on the intensity. For drug testing, animals were divided into following groups of 6 guinea pigs each.

Group I Served as vehicle control and received 1 ml of distilled water orally half an hour before exposure to UV.

Group II received 250 mg/kg body weight of sodium pyruvate orally half an hour before exposure to UV.

Group III 50 mg of 5% w/w sodium pyruvate ointment was applied on both the circular areas of the flank half an hour before exposure to UV.

Group IV received 3 mg/kg body weight of naproxen orally, one hour before exposure to UV.

Statistical analysis

Kruskal–Wallis test was used to analyse the data and $P<0.05$ was considered to be significant.

RESULTS AND DISCUSSION

The erythema indices after sodium pyruvate in comparison to naproxen are shown in Table I.

In other studies sodium pyruvate has been found to be effective against carrageenan induced oedema and Freund's adjuvant induced arthritis model in rats (unpublished data). This prompted us to study its role against radiation (UV) induced erythema of guinea pig skin.

UV radiation induced free radical oxidative stress is thought to play a major role in skin damage (3, 4). The exposure of guinea pig skin to ultra violet radiation for 2 min evokes a prolonged inflammatory

TABLE I : Comparative erythema index after sodium pyruvate and naproxen against uv-induced erythema of guinea pig skin.

Group	*Dose and route of administration*	*Erythema index at different time intervals after uv exposure*		
		1 h	*2 h*	*4 h*
Control (distilled water)	0.5 ml, oral	1.00	1.80	2.00
Sodium pyruvate	250 mg/kg, oral	0.66*	1.00*	1.16*
Sodium pyruvate	50 mg of 5% ointment, topical	0.30*	0.83*	1.60*
Naproxen	3 mg/kg, oral	00*	0.66*	1.33**

Each value represents the mean erythema index of 6 animals.
* = P<0.05 ** = P<0.01

response. A single exposure of the skin to ultra violet light induces an erythematous response and an increase in vascular permeability. Erythema development reaches a maximum by 4 hours. Though the time course of the permeability response appears to be different from that of erythema development. At 4 hrs after UV exposure, the exposed sites exhibit an intense redness (grade-II). Torrent et al have suggested the use of UV induced erythema model for the development of NSAIDs for possible systemic use (5). The involvement of free radicals and related species due to UV radiation is a well known phenomenon. In our study naproxen was selected as a standard drug, because it exhibits both anti-inflammatory and antioxidant properties (6). Naproxen was administered 1 hour before uv-exposure because it is reported to reach peak plasma concentration within 2–4 hrs of administration. In general, the pattern of UV induced inflammation is similar to that evoked by other types of injuries, for example – experimental bacterial infection (7), thermal injury (8), superficial chemical burns (9) etc.

Pretreatment with oral as well as topical sodium pyruvate, delayed the onset and progression of erythema development as evident from the results in Table I. The anti-erythemic activity of sodium pyruvate at 250 mg/kg dose level after 4 hours of UV–B challenge was almost comparable to that of standard naproxen (3 mg/kg).

Free radicals generation, mainly the reactive oxygen species superoxide radical, hydroxyl radical and hydrogen peroxide at the site of inflammation is well established (10) and pyruvate is recognised to have free radical scavenging properties (11–14). The observed efficacy of sodium pyruvate against uv-induced erythema seems probable due to its antioxidant and UV-B radiation absorbing properties. It may act directly as scavenger of hydrogen peroxide and activate pyruvate dehydrogenase.

In addition to anti-inflammatory activity sodium pyruvate was also evaluated for any

effect on rat blood pressure, guinea pig ileum and rat uterus but it was found to have no effect on any of these.

The findings of the present study suggest that sodium pyruvate is a safe drug which significantly delays UV-induced erythema of guinea pig skin and therefore may act as a potential sunscreening agent. The encouraging results of this study give an idea for developing sodium pyruvate as an adjuvant in mild inflammatory conditions which directly involve the generation of free radicals, However, for cosmetic point of view, further studies are needed to prove its potential value as a sunscreening agent.

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