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In-vivo valuation of pharmacologically beneficial tendency in beta-carotene

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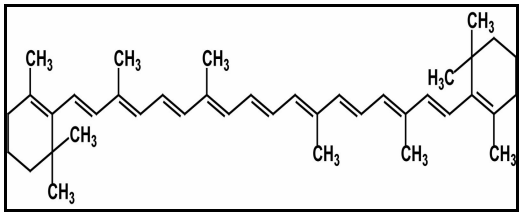
Abstract : β-carotene a member of carotenes, is an organic red-orange pigment present in plants. β-carotene is a precursor of vitamin A. In the body, β-carotene is converted to vitamin A (retinol). β-carotene is also known to have antioxidant activity[1]. Current study is aimed at exploring the pharmacological activities of β-carotene. This was achieved by examining its analgesic, antipyretic and ulcerogenic properties with different experimental models in mice. A non-steroidal anti-inflammatory drug (NSAID), indomethacin (3 mg/kg b.wt.;i.p.) was used as standard for the purpose of comparison. It was found that β-carotene possesses significant ($P<0.05$) analgesic and antipyretic effect compared to indomethacin. Animals administered orally with β-carotene (10 mg/kg b.w.) after 16 hours of fasting showed absence of gastric damage, whereas indomethacin administered rat showed gastric damage.
Keywords: Antioxidant, Antipyretic, Analgesic, β-carotene, supplement.

Introduction

β-carotene also known as Provitamin A is one of the group of red, orange, and yellow pigments called carotenoids with pro-vitamin A (retinol) activity. It is a member of the carotenes, which are terpenoids (isoprenoids), synthesized biochemically from eight isoprene units and have 40 carbons[2]. Carotene in plants is found in two forms alpha and beta. β-carotene is distinguished by having beta rings at both the ends of the molecule[3]. β-carotene does not contain oxygen and isfat-soluble.β-carotene can be found in fruits, vegetables, and whole grains.β-carotene is considered a safe source of vitamin A because in the body β-carotene gets converted into vitamin A (retinol).Vitamin A is needed for good vision, a strong immune system, and for healthy skin and mucous membranes[4].β-carotene is an effective antioxidant. Epidemiologic evidence indicates that carotenoid (β-carotene) rich fruits and vegetables, are associated with a reduced risk of lung cancer, heart disease, cataracts and age related macular degeneration, rheumatoidarthritis, high blood pressure[5].



Chemical structure of β-carotene

The present study is conducted to assessthe analgesic, antipyretic and ulcerogenic properties of β-carotene at different doses in standard rat model. Indometacin, which is a non steroidal anti-inflammatory drugs was used for comparison purpose[6].

Materials and methods

Animals

Wistar rat of female sex, with a mean body weight of 200g was used for the experiments. The animals were procured from the Animal house of VIT University Vellore. Ratswere maintained at temperature controlled room with 12 hr dark-light cycle. They were fed with standard pellet diet and water *ad libitium*.

Test drug

The commercially available β-carotene (soft gel capsules, vitamin A- 25000 IU) was purchased from Nature's Bounty INC Bohemia, U.S.A.Indomethacin was purchased from Tamil Nadu Dadha Pharmaceuticals Ltd., Chennai, India. Fresh solution was prepared before each experiment. All other reagents used were standard laboratory reagents of analytical grade and were purchased locally.

Dosage

Based on preliminary studies with different dosage of β-carotene it was found that 10 mg/kg b.wt. produced significant anti-inflammatory effects. No mortality was observed in mice during our examination period.

Analgesic Test: Acetic acid induced writhing method.

Analgesic test was performed by the method of Witkin et.al (1961)[7]. β-carotene (10mg/kg b.wt) and indomethacin (3mg/kg b.wt) were administered orally prior to the injection of acetic acid. After 30 min writhing effect was induced by intraperitoneal injection of 0.6% solution of acetic acid (10ml/kg b.wt). Each rat was placed in glass cages and the number of stretching per animals was noted during the period of 30 minutes. Reduction in number of writhing of treated group was compared with writhing count of control group.

Hot- Plate test

Hot plate reaction time in rat was tested by the method of Williamson et.al (1996)[8]. Mice were placed on a hot plate maintained at temperature of 55ºC to check the temperature withstanding power of the animal. The pain threshold is considered to be reached when the animals lift or lick their paws or jump out of the beaker. β-carotene (10mg/kg b.wt) and indomethacin (3mg/kg b.wt) were administered orally and after a period of 30 minutes they were tested for paw licks or jump response to the hot temperature using stopwatch.

Antipyretic Test: Yeast induced pyrexia

Antipyretic test was performed by the method of Mukerjee et.al (1996)[9]. The normal body temperature of rats was noted initially and pyrexia was induced by subcutaneous treatment with 10ml/kg of aqueous suspension of baker's yeast. After 18 hrs the rise in temperature was noted. β-carotene (10mg/kg b.wt) and indomethacin (3mg/kg b.wt) were administered orally and rectal temperature was noted after every 1 hr upto 22 hours of the experiment.

Ulcerogenic Test

Ulcerogenic test was performed by the method of Cashin et.al (1977)[10]. The animals were fasted for 16 hrs. At the end of fasting β-carotene (10mg/kg b.wt) and indomethacin (3mg/kg b.wt) were administered orally to check the ulcerogenic activity. 3 hour after the administration of drug the animals were killed and the stomachs were removed, opened along the great curvature and the gastric mucosa was washed with normal saline and scored according to the scale, 0: no lesion; 0.5: hyperemia; 1: one or two lesions; 2: sever lesions; 3: very sever lesions; 4: mucosa full of lesions.

Results

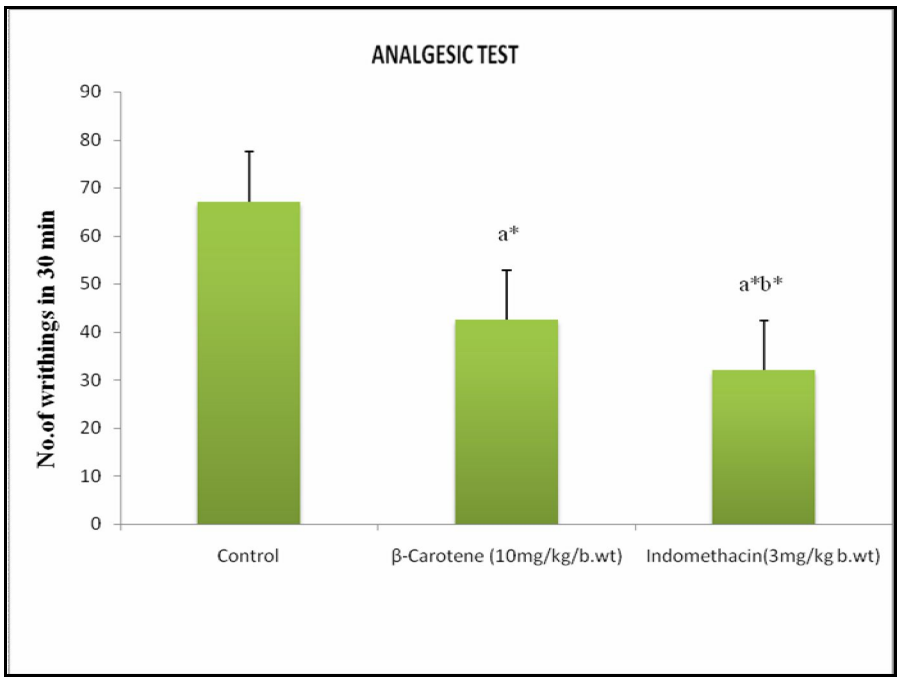
Statistical analysis

Results were expressed in mean $\pm$ S.D and statistical analysis was performed using ANOVA to determine differences between group followed by student's Newman-Keul's test.$P<0.05$ implied significance.

Pharmacological activities like analgesic, antipyretic and ulcerogenic activities of β-carotene were determined in rat.

Analgesic test

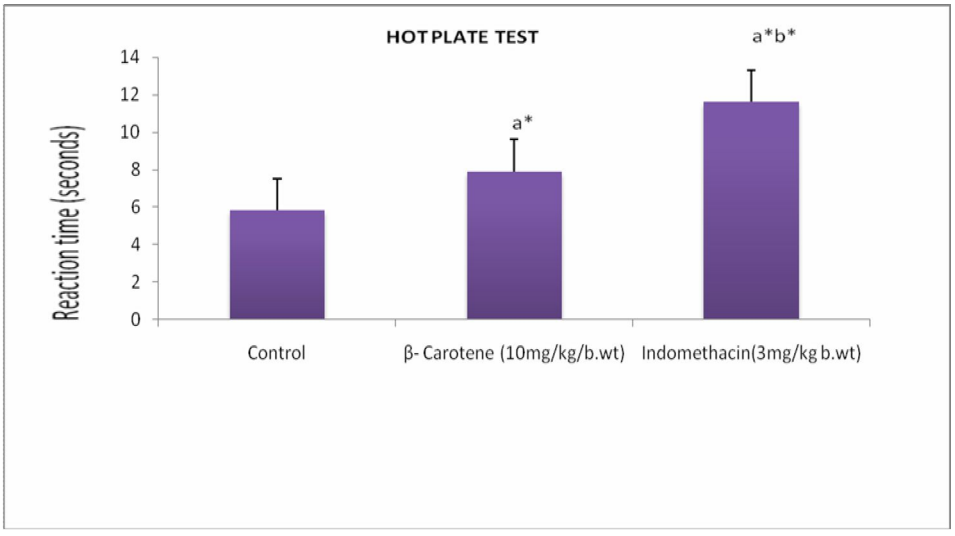
The analgesic activity of β-carotene was investigated by acetic acid induced writhing test in mice. The maximum number of writhing after acetic acid administration was observed in control group. The writhing count decreased significantly after administration of β-carotene and indomethacin. This reduction was dose related and found to be maximum with 10 mg/kg.b.wt.



Comparisons were made with control groups. Values are expressed as mean ± S.D (n=6). Symbols represents statistical significance at * p < 0.05.

Hot-plate test

In this test, rats administered with β-carotene showed significant ($p<0.05$) dose dependent delayedresponse time in pain threshold and the results werecomparable to standard reference drug indomethacin. It shows the analgesic activities of β- carotene and indomethacin.



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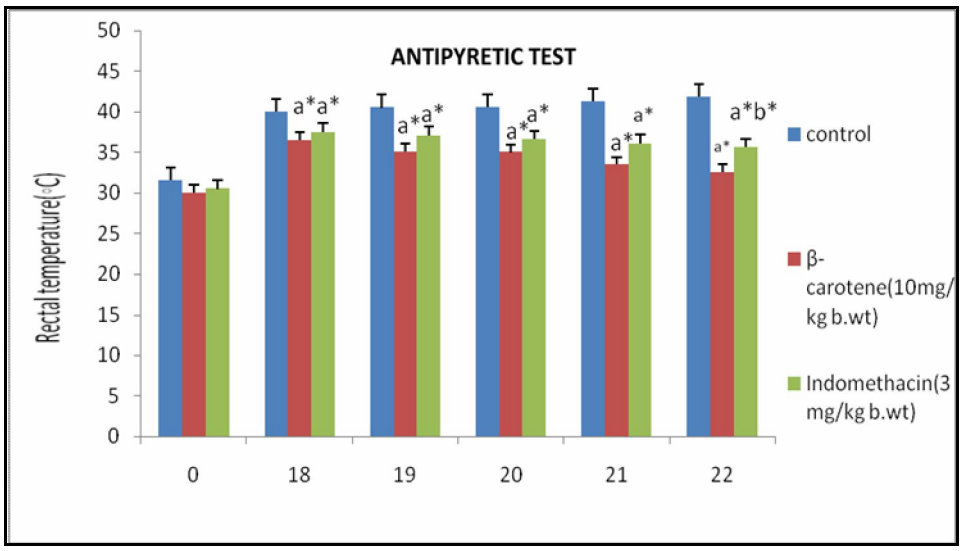
Antipyretic test

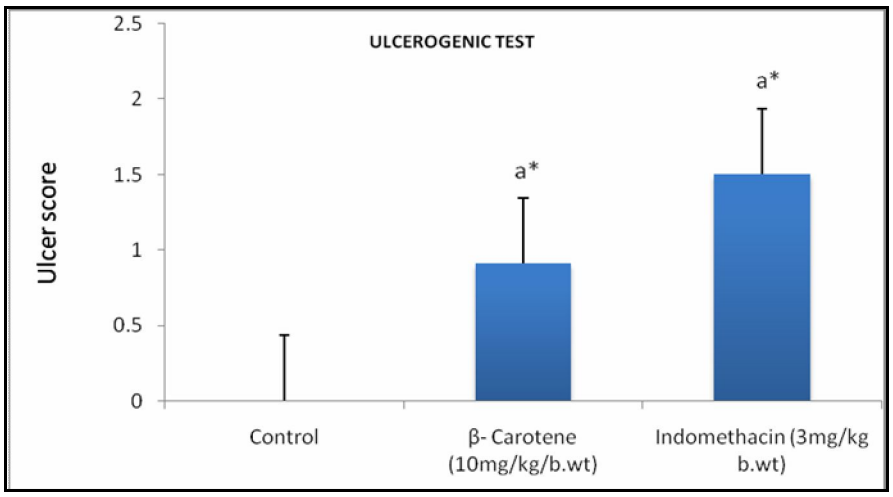
A significant increase in rectal temperature of control group was observed in mice after 18 hours of the administration of yeast. There was dose dependent decrease in rectal temperature in β- carotene (10 mg/kgb.wt) treated group of rat. In case of indomethacintreated rat, the rectal temperature was more as compared to β-carotene treated group.



Comparisons were made with control groups. Values are expressed as mean ± S.D (n=6). Symbols represents statistical significance at * p < 0.05.

Ulcerogenic test

Rat treated with β-carotene (10 mg/kg.b.wt.) showed dose related decrease in gastric lesions as compared to standard anti-inflammatory agent indometacin. Indomethacin (3 mg/kg b.wt) treated rat produced significant gastric lesions.



Comparisons were made with control groups. Values are expressed as mean ± S.D (n=6). Symbols represents statistical significance at * p < 0.05.

Discussion

There are various drugs available which are currently in use for anti-inflammatory disorders. These drugs show analgesic and antipyretic effect that is often associated with causing gastric damage[11]. Therefore, in the present study an attempt was made to evaluate the analgesic and antipyretic effect of β- carotene and to know the ulcerogenic effects of β- carotene.The results show that analgesic and anti-inflammatory effects of β-

carotene are comparable with indomethacin, which is a non-steroidal anti-inflammatory drug (NSAID)[12]. The analgesic effect of β-carotene was evaluated using acetic acid induced writhing response and hotplate reaction time in rat.The acetic acid writhing test is a non-discriminatory anti-nociceptive model[13]. It is used to screen both peripheral and centrally acting analgesic activity.Nerve endingswere excited due to the painful response and acuteinflammation, because of release of prostaglandins in the peritoneal area.NSAIDs can reduce number of writhes by blocking prostaglandins enzyme inperipheral tissues[14]. Analgesic effect of β-carotene may be due to blockage of the local level of prostaglandins. Therefore it suggests that β-carotene has inhibitory action in the synthesis of prostaglandin biosynthesis[15]. The determination of writhing test alone doesnot confirm that this effect is related with central analgesicsubstances. The hot plate reaction test is used to screen the central nervous system acting analgesic activity of a drug[16]. In the hot plate test, a significant analgesic action was showed by β-carotene after 30 minutes of administration.Theresults showed significant analgesic effect in acetic acidwrithing response and hot plate reaction test by β-carotene.This confirms that analgesic effects of β-carotene are resultantof both peripheral and central acting mechanisms.

Antipyretics are drugs which regulate elevated body temperature[17]. In yeast induced fever, production of prostaglandins sets the thermoregulatory center at higher temperature and this is regulated by hypothalamus. Prostaglandin production is inhibited by antipyretic activity[18],[19]. Administration of antipyretic compounds after 18 hours of yeast injection is a common method used to investigate the pyretic effect[20]. In the present study β-carotene showed significant reduction in rectal temperature similar to indometacin. So this shows that beta carotene has inhibitory effect on prostaglandin biosynthesis. Anti-inflammatory agents exhibit their activity through inhibition of biosynthesis of prostaglandin which induces gastric lesions[21]. The main side effects of non steroidal anti-inflammatory drug are to produce gastric lesions and thus ulcers[22]. In the present study, administration of β-carotene after fasting produced less number of gastric lesions as compared to standard drug indometacin. So this indicates that beta carotene has anti ulcerogeneic activity.

Conclusion

The results of present study show that β-carotene possesses significant ($P<0.05$) analgesic, antipyretic and anti ulcerogenic properties. It is evident that β-carotene displayed better activities compared to the control drug indomethacin. However, further investigation is required to elucidate the exact mechanism which underlies the aforementioned beneficial effects of β-carotene.

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