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ORIGINAL ARTICLE **OPEN ACCESS**

Effect of mosinone-a on membrane bound enzymes status in DMBA induced hamster buccal pouch carcinogenesis

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ABSTRACT
The aim of the present study was to investigate the protective effect Mosinone-A on membrane bound enzymes status during 7,12-dimethylbenz[a]anthracene (DMBA) induced oral carcinogenesis. The protective effect of Mosinone-A was assessed by measuring the status of, membrane bound enzyme activity. Oral squamous cell carcinoma was induced in the buccal pouch of Syrian golden hamsters by painting with 0.5% DMBA in liquid paraffin thrice a week for 14 weeks. The levels membrane bound enzyme activity were analyzed by using specific colorimetric methods. We observed 100% tumor formation in DMBA painted hamsters. The activity of membrane bound enzymes decreased Oral administration of Mosinone-A at a dose of 2mg kg⁻¹bw significantly prevented the tumor formation as well as normalized the biochemical variables in DMBA painted hamsters. Our results thus demonstrate the *protective effect of Mosinone-A on during DMBA induced oral carcinogenesis.*
Keywords: Cell membrane,DMBA, Mosinone-A,buccal pouch, Oral cancer, carcinoma,liquid paraffin.

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INTRODUCTION

Carcinogenesis is a multi-step process involving several mutations, each of which results in discrete changes in the cellular metabolism [1]. Oral squamous cell carcinoma is predominantly a disease of human population in the fifth to eighth decades of life. The incidence and mortality rate of oral cancer vary widely across the world. However, the higher incidences of oral cancer are reported every year from developing countries, particularly from India [2]. Epidemiological studies have shown that chewing of betel quid with tobacco is the major etiological factor of oral carcinogenesis in India [3].The importance of tumor markers for the detection of malignancies and its prognosis has prompted the investigation of the possible biochemical markers of several malignancies. DMBA-induced experimental oral cancer is the most widely-accepted experimental model for studying chemoprevention of oral cancer, since it has several morphological and histological similarities with human oral carcinoma [4].The membrane bound enzymes such as Na^+/K^+-ATPase, Mg^{2+}-ATPase and Ca^{2+}ATPase are responsible for the transport of sodium/potassium, magnesium and calcium ions across the cell membranes at the expense of ATP by hydrolysis [5]. Na^+/K^+-ATPase is an important regulator of intracellular electrolyte levels in almost all mammalian cells. The plasma membrane Ca^{2+}ATPase is an essential regulator of free intracellular calcium and magnesium, an abundant cation in cells, is involved in many biological functions. ATP strongly binds to Mg^{2+} and exists as an Mg^{2+}ATP complex in cells. Moreover, it has been known that intracellular Mg^{2+} concentration changes in response to extracellular stimulus and, in some cases, intracellular Mg^{2+} change is accompanied by intracellular Ca^{2+} change [6]. However, no scientific reports were available on the literature for altered the levels of lipids membrane bound enzymes and osmotic fragility in DMBA induced hamster buccal pouch carcinogenesis. Therefore, the present investigation was undertaken to study the effects of Mosinone-A on lipid profile, membrane-bound enzymes and osmotic fragility in hamster buccal pouch carcinogenesis.

MATERIALS AND METHODS

Animals: Male golden Syrian hamsters 8–10 weeks old weighing 80-120g was purchased from National Institute of Nutrition, Hyderabad, India and was maintained in Central Animal House, Rajah Muthaiah Medical College and Hospital, Annamalai University. The hamsters were housed five in a polypropylene

cage and provided standard pellet diet and water *ad libitum*. The hamsters were maintained under controlled conditions of temperature and humidity with a 12 h light/dark cycle. The hamsters were maintained as per the principles and guidelines of the ethical committee for animal care of Annamalai University in accordance with Indian National Law on animal care and use.

Chemicals

The carcinogen, DMBA, was obtained from Sigma-Aldrich Chemical Pvt. Ltd., Bangalore India. All other chemicals used were of analytical grade.

EXPERIMENTAL DESIGN

A total number of 40 hamsters were randomized into four groups of 10 hamsters each. Group 1 hamsters were served as control and were painted with liquid paraffin alone thrice a week for 14 weeks on their left buccal pouches. Groups 2 and 3 hamsters were painted with 0.5% DMBA in liquid paraffin thrice a week for 14 weeks on their left buccal pouches. DMBA painting in hamster's buccal pouches was done by using number 4 painting brush, which leaves approximately 0.4mg DMBA on hamster buccal pouch in each application [7-8]. Group 2 hamsters received no other treatment. Group 3 hamsters were orally administered Mosinone-A at a dose of 2mg/kg bw, starting one week before the exposure to the carcinogen and continued on days alternate to DMBA painting, until the scarification of the hamsters. Group 4 hamsters received oral administration of Mosinone-A alone throughout the experimental period. The experiment was terminated at the end of 15 weeks and all hamsters were sacrificed by cervical dislocation.

STATISTICAL ANALYSIS

The data are expressed as mean ± SD. Statistical comparisons were performed by One-way analysis of variance (ANOVA), followed by Duncan's Multiple Range Test (DMRT)[9]. The results were considered statistically significant if the p values were less than 0.05

RESULT

Table 1. Shows the activities of membrane bound enzymes (ATPase) in erythrocyte membrane and plasma, of control and experimental animal in each group. The decrease in the Na^+/K^+ ATPase and Mg^{2+}-ATPase and Ca^{2+}-ATPase activity in cancer bearing hamsters when compared with control animals. Oral administration of Mosinone-A normalized the altered levels of membrane bound enzymes in pre-initiation phase and significantly improved the activities in post initiation phase, animals treated with Mosinone-A alone showed (group5) no significant differences in the levels of membrane bound enzymes as compared to control animals.

Table 1 The activity of membrane bound enzymes in erythrocyte membrane of control and experimental hamsters in each group (n=10)

S.NO	Treatment Groups	Na^+K^+ ATPase	Ca^{2+}ATPase	Mg^{2+} ATPase	Mean corpuscular fragility
1	Control	0.77 ± 0.08^a	0.72 ± 0.08^a	0.74 ± 0.08^a	0.45 ± 0.05^a
2	DMBA	0.34 ± 0.04^b	0.23 ± 0.02^b	0.32 ± 0.04^b	0.72 ± 0.08^b
3	DMBA+Mosinone-A (2 mg/ kg b.wt)	0.55 ± 0.06^c	0.48 ± 0.04^c	0.57 ± 0.06^c	0.56 ± 0.06^c
4	DMBA→Mosinone-A (2 mg/ kg b.wt)	0.45 ± 0.05^d	0.32 ± 0.05^d	0.48 ± 0.05^d	0.63 ± 0.07^d
5	Mosinone-A alone (2 mg/ kg b.wt)	0.76 ± 0.07^a	0.71 ± 0.07^a	0.75 ± 0.08^a	0.44 ± 0.05^a

Values are expressed mean ± SD. Values not sharing a common superscript significantly differ at $p < 0.05$ (DMR

CONCLUSION

Membrane bound enzymes play an important role in biological functions which include membrane composition and regulation, energy metabolism, and signal transduction. Lipids have been found to be involved in many human diseases including cancer. Several prospective and retrospective studies have shown an inverse association between blood Membrane bound enzymes and different cancers [11-10]. Researchers have reported association of plasma/serum membrane bound enzymes with different cancers. An earlier study reported that lipids might primarily affect gonads and subsequently higher estradiol secretion could influence the development of malignancies (Jauhiainen and Ehnholm, 2005). In Neoplastic disease is related to new growth, there is a greater utilization of Membrane bound enzymes [12]. The abnormalities in Membrane bound enzymes produce number of pathological diseases including cancer. Membrane bound enzymes accumulation has been reported in various solid tumors, including prostate cancer and oral cancer. In addition, cholesterol metabolism is dysregulated in many

malignancies, including myeloid leukemia, lung, and breast cancers [13]. The protection of membrane potential is importance in the treatment of disease processes. The membrane bound enzymes such as Na^+K^+ATPase are responsible for the transport of sodium/potassium across the cell membranes at the expense of ATP by hydrolysis [14]. The activity of ATPase in erythrocyte membrane and surrounding tissues has been found to be inhibited in tumor bearing animals. Oxidative damage to membrane bound enzymes has been assumed to be crucial for cell lysis [15]. A decrease in membrane bound Na^+K^+ATPase in DMBA painted hamsters suggest that the membrane permeability was drastically altered during DMBA induced oral carcinogenesis. Oral administration of Mosinone-A significantly improved the activity of membrane bound enzyme activity in the DMBA painted hamsters.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

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