Introduction
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In today’s developed world the problem of cancer is increasing and is now second only to cardiovascular diseases as a cause of death, affecting millions of people throughout the world. Various disciplines come into play in the multifaceted attack on the enigmatic origins of cancer. Carcinogenesis is a multistage process and depends on multiple factors. The combined effect of stimulatory factors (e.g., hormones, cytokines), stress mediators (oxygen radicals) and exogenous aggressions (viruses, radiation and chemical carcinogens) can affect the control of cellular proliferation and lead to tissue transformation. For more than half a century numerous proposals have been advanced for the mode of action of carcinogens. A substantial body of evidence has been produced that implicates oxidative stress in many aspects of oncology, including formation of reactive oxygen species (ROS) by the major classes of carcinogens, cancer stages and oncogene activation.

Psychological stress, a common phenomenon, generally a state of disturbed homeostasis, harmony and equilibrium is attracting increasing attention due to its implication in wide range of diseases including cancer. Increasing evidence suggests that stress and the ability to cope with stress may play a role in malignant transformation and tumor progression. Although the studies examining the effect of psychological stress on the production of ROS have yielded inconsistent results, it has been shown that exposure to stress situations can stimulate numerous pathways leading to increased production of free radicals. These free radicals, as already known, generate a cascade producing lipid peroxidation, protein oxidation, DNA damage and cell death and contribute to the occurrence of pathological conditions. Stress may also impair antioxidant defenses, leading to oxidative damage, by changing the balance between oxidant and antioxidant factors. Since the involvement of oxidative stress in cancer induction and its subsequent development, and associated molecular mechanisms is becoming increasingly clear, the influence of stress-inducing conditions on cancer development has been subject of several investigators, both at clinical and experimental level. However results are contradictory as both exacerbation and attenuation of tumor development by stress has been reported. For example, foot shock or electric shock enhanced tumor development, while various other stresses inhibited the growth of both transplanted and chemically induced tumors in rats. Human studies have focused mainly on the effect of psychosocial
factors including stress on prognosis in patients who already have cancer, while very limited information is available on any possible direct role of stress in the development of neoplasia. Immobilization, used in the present study is a classic method that has long been used to study the impact of physical as well as psychological stress on disease process in experimental animals.

To study the genetic and biological changes involved in tumor promotion, mouse or rat skin carcinogenesis model has become very useful and was employed in the present study using the complete carcinogen 7,12-dimethylbenz (a) anthracene (DMBA). DMBA is a polycyclic aromatic hydrocarbon present in the environment as a product of incomplete combustion of complex hydrocarbons. It is an indirect carcinogen and is metabolized by cytochrome P4501B1 to form toxic metabolites and ROS. These ROS produce deleterious effects by initiating lipid peroxidation directly or indirectly by acting as second messengers for the primary free radicals and the toxic metabolites of DMBA bind to adenine residues of DNA causing damage. Persistent DNA damage can result in either arrest or induction of transcription, induction of signal transduction pathways, replication errors, and genomic instability, all of which are seen in carcinogenesis.

Another field that has attracted lot of attention, since the proposition of different theories of cancer, is cancer chemoprevention. Due to the growing evidence that antioxidants may prevent or delay the onset of some types of cancers, many compounds with antioxidant properties have been studied for prevention as well as cure of different cancers and were found to be effective in most of the cases. However, the prevention or cure of disease in almost every case depends on the response of the host to the chemotherapy. It is widely believed that antioxidants help maintain human health by decreasing oxidative damage to key biomolecules. However, the antioxidant status in general and in vivo in particular has been shown to be modulated by exposure to stressful events. Animal studies have shown that exposure to rotational stress decreases the antitumor effects of chemotherapeutic drugs in terms of tumor burden, extent of metastasis and survival time.

The present study has been carried out to examine the effect of stress on the early stages of carcinogenesis in terms of biochemical parameters and in vivo antioxidant status of rats. The work done has been divided into two parts. First part deals with the effect of
Introduction

stress on the antioxidant status of experimental animals exposed to chronic restraint stress via the measurement of alteration of various biochemical parameters considered as markers of oxidative stress such as the activities of superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST) and the levels of glutathione (GSH), glucose, malondialdehyde (MDA), uric acid etc. The marker enzymes of liver function were also analyzed in both the liver tissues and circulation. Moreover, the role of stress in the early stages of DMBA induced carcinogenesis was also assessed. The effect of mode of infusion of DMBA i.e., oral and topical was also studied on alteration of above mentioned biochemical parameters in the presence and absence of restraint stress. Further studies were carried out to evaluate the effect of restraint stress on DNA damage in experimental animals, alone and in context of DMBA induced carcinogenesis.

In the second part, chemopreventive studies were carried out using well-known antioxidants- melatonin and resveratrol. The chemopreventive effects of both the drugs were evaluated on DMBA induced skin carcinogenesis in the presence and absence of stress in terms of DNA damage, fluorescent studies and alteration of various biochemical parameters and antioxidant enzymes. The experimental model currently employed might provide an insight at the most basic level of cell mutation, for investigating the effect of both physical and psychological stress on the etiology of DMBA induced carcinogenesis. This study may aid in the understanding of cancer initiation and can serve as a useful tool for further studies aimed at the development of interventions for disease prevention by identifying the relation between psychological factors and carcinogenesis.