PREFACE

The recent World Cancer Report, the most comprehensive global examination of the disease to date, released on 3rd April 2003, by the World Health Organization (WHO), predicts that cancer rates could further increase by 50% to 15 million new cases in the year 2020. In the year 2000, malignant tumors were responsible for 12% of the nearly 56 million deaths worldwide from all causes. In 2000, 5.3 million men and 4.7 million women developed a malignant tumor and altogether 6.2 million died from the disease. The report also reveals that, cancer has emerged as a major public health problem in developing countries, matching it's effect in industrialized nations (www.who.int/medicentre/news/releases/2003/pr27/en/).

In developed countries, the probability of being diagnosed with cancer is more than twice as high as in developing countries. However, in rich countries, some 50% of cancer patients die of the disease, while in developing countries, 80% of cancer victims already have late-stage incurable tumors when they are diagnosed, pointing to the need for much better detection programs. The main reasons for the greater cancer burden of affluent societies are the earlier onset of the tobacco epidemic, the earlier exposure to occupational carcinogens and the western nutrition and lifestyle. However, with increasing wealth and industrialization, many countries undergo rapid lifestyle changes that will greatly increase their future disease
The use of drugs in the treatment of malignancies is of much more recent origin, than the use of surgery or radiation therapy. The first recorded clinical trial of a chemotherapeutic agent took place in 1942, when nitrogen mustard was given to a patient with advanced lymphosarcoma (Goodman et al., 1946). A dramatic, but unfortunately brief tumor response was achieved in this patient. Later, in the same decade, Sidney Farber observed, what he termed an “acceleration phenomenon”, in a retrospective analysis of children with acute leukemia treated with folate conjugates. This experience led him to a trial of folate antagonists and in 1948, he reported dramatic responses in ten of sixteen children, treated with the folate antagonist, Aminopterin (Farber et al., 1948).

Since these initial studies, the field of chemotherapy has grown tremendously, so that at the present time, a wide spectrum of human malignancies can be affected by the administration of antineoplastic drugs.

The progress that has been made, since the first use of nitrogen mustard in 1942, has been remarkable. Some diseases are curable and some are eminently treatable by chemotherapy. Unfortunately, much still remains to be accomplished. The currently used drug regimens for many malignancies are toxic to normal host tissues and if improperly used can be lethal.
Selective toxicity to tumor cells is still an elusive goal.

The alkylating agents, as a group have long held the interest of both, practical cancer chemotherapists and experimental pharmacologists. They have assumed this position of importance, because they were among the first clinical agents of recognized value and because their study has increased our understanding of cancer chemotherapy in general. Many of the alkylating agents are related to mustard gas first used for chemical warfare in World War I. At that time, it was noted that limited exposure to this agent caused bone marrow suppression, somewhat similar to that produced by radiation.

The alkylating agents and nitrosoureas are important, because of their ability to destroy neoplastic tissue, but their specificity for malignant cells is far from complete and they exhibit a wide range of toxicities when administered to whole animals. Apart from genotoxic and cytotoxic effects, they also exhibit, bone marrow suppression, nausea, vomiting alopecia, interference with spermatogenesis and other less frequently encountered toxicities. These side effects appear to represent the increased cytotoxicity of these agents for rapidly proliferating tissue and they can be explained in terms of damage to DNA.

Several anticancer drugs have entered the chemotherapy market, of
which, hardly any information on the genotoxic, cytotoxic and biochemical effects is known. It is quite natural that, the rate at which these drugs are flooding the present day competitive market, it is hardly possible for any manufacturer to analyse them thoroughly. Apart from the above, the drug manufacturers' primary concern lies in the cure of a particular disease, cancer – in the present context and not on the side effects of the drugs.

Hence, a humble attempt has been made, to analyse the cytotoxic, genotoxic and biochemical effects of a few selected anticancer drugs, in the present investigation.