CHAPTER 1

# MEDICINAL PLANTS AND CANCER

Roughly one person in five in the prosperous countries of the world is at a risk of dying of cancer. Cancer is the disease which comes next to heart diseases in fatality count or mortality. When Richard M. Nixon signed the National Cancer Act in 1971, he committed the US to a 'war' on cancer. Since then, the battle has been waged around the world laboratories, hospitals, our town houses etc. As a result, death toll from some of the greatest cancers has begun to come down, at least in some segments of the population. Some researchers have started to view cancer as a disease that might be managed over the long term, as it cannot be cured. Eradicating every omnion cell from a cancer patient's body is a difficult goal and in many cases it may not be possible or necessary. The day of complete cancer management may not be here in the near future, but tools that medicine has now are a start. Of course ultimate goal remains unchanged, "We have to keep our eyes on the prize, which is to kill the cancer."

To understand cancer and to derive rational ways to treat it, we have to understand both the inner workings of the cells and their social interactions in the tissues of the body. Thus cancer research effort has profoundly benefited a much wider area of medical knowledge than that of cancer alone.

'Cancer' refers to more than 100 forms of the disease. Almost every tissue in the body can spawn malignancies and some even yield several

types of it. So cancer is not a single disease but a group of diseases with one thing in common.

Normal cells reproduce only when instructed to do so by other cells in their vicinity. Such unceasing collaboration ensures that each tissue maintains a size and architecture appropriate to the body's needs. Cancer cells, violate this scheme, they become deaf to the usual controls on cell division or proliferation and follow their own internal agenda for propagation (Hyperplasia). They also possess an even more insidious property—the ability to migrate from the site, where by they invade nearby tissues and form masses at distant sites in the body (Metastasis). Tumours composed of such malignant cells become more and more aggressive over time and they become lethal when they disrupt the tissues and organs needed for the survival of the organisms as a whole.[103]

Two classes of genes which together constitute a small proportion of the full genetic set and control the cell division and proliferation and play major roles in triggering cancer[104]. Proto-oncogenes encourage the cell enlargement and division where as tumour supressor genes inhibit it. Activation of oncogenes or inactivation of tumour suppressor genes (due to mutation) can cause excessive multiplication of normal cells which may result in cancer. Mutations may be due to chemicals, viruses, radiation etc.

It is estimated that a majority of cancers are caused or promoted by life style factors that are controllable at the individual or society level or both.[105] Besides carcinogenic viruses and chemicals, risk factors such as diet[106], radiation[107], some occupational[108] and drug exposure[109]and alcohol consumption[110] have all been implicated in cancer causation. But the most demonstrated risk factor is tobacco use-particularly smoking.[111]

Although major forms of treatment of cancer are still considered to be surgery and radiation, the use of chemotherapeutic agents can often provide

temporary relief of symptoms, the prolongation of life and occasionally cures. A successful anti cancer agent should kill or incapacitate cancer cells without causing excessive damage to normal cells. Synthesis of modifications of known drugs continues as an important aspect of research, but the relatively small improvements over prototype drugs, which have remitted from the vast amount of synthetic work are discouraging. There exists a need for new prototypes, new templates to use in the design of potential chemotherapeutic agents and natural products are providing such templates. Recent studies of tumour inhibiting compounds of plant origin are yielding an impressive array of novel structures. Many of these structures are extremely complex, and it is most unlikely that such compounds will be synthesised in empirical approaches to new drugs[112].

Plant materials have been used in the treatment of malignant diseases like cancer for centuries, describing plants used against cancer lists over 1400 genera. Recent phytochemical examination of plants which have a suitable history of use in folklore for treatment of cancer has indeed often resulted in the isolation of principles with antitumour activity. Major research programmes are being undertaken in a number of laboratories in various parts of the world for screening plant extracts for antitumour activity under the auspices of United States National Cancer Institute (NCI), Some 3000-4000 plant samples representing 2000 species are screened each year. Different parts of the plant—seeds, leaves, roots, etc.—are separately examined wherever possible.[112] For the detection of anticancer compounds random plant selection was adopted for the screening of plants for biological activity. The following table gives a description of certain tumour inhibitory principles isolated as natural products.

| Plant Name | Chemical Compound (Product) |
|---|---|
| 1. *Camptothein accuminata* | Camptothein |
| 2. *Acronychia baueri* | Acronycine |
| 3. *Vinca rosea (Catharanthus roseus)* | Vincristine and vinblastine |
| 4. *Tylophora crebiflora* | Tylocrebine |
| 5. *Thalictrum dasycarpum* | Thalicarpine |
| 6. *Cyclea peltata* | Tetrandine |
| 7. *Tripteryguim wilfordei* | Triptolide and tripdiolide |
| 8. *Podophyllum pellatum* | $\alpha$ and $\beta$-peltalin |
| 9. *Crotalaria spectabilis* | Monocrotaline |
| 10. *Colchicum speciosum* | Colchicine |

The activities of many of the drugs currently in use in cancer chemotherapy can probably be ascribed to inhibition of nucleic acid synthesis, but mechanisms of action differ widely (Like intercalating agents, antimetabolites, mitotic inhibitors etc.). Even if no natural products themselves attain this status, the benefits of this research will probably be measured in terms of our further understanding of the biochemical phenomena of cancer and the development of useful drugs using natural products as the chemical templates. The phytochemical investigations of the natural products from plants may vary as the concentration of the active constituents can change due to many factors namely climate, place, soil nutrients, season of collection etc Moreover general studies done with plants are carried out in such a manner as to conserve only chemically more stable materials possibly destroying the less stable but more potent active agents[113]. Plant synthesises a variety of organic compounds which can provide anti- cancer activity. The main task is to isolate and purify them so

that the negative effects (toxic effects) of any compounds can be avoided. The old saying that "a natural remedy exists for every disease" may have some core truth in it and deserves further exploration utilising all modern technology.

Although India is known to be extremely rich in medicinal plants, no comprehensive, systematic and controlled survey of antineoplastic activity has so far been undertaken. CDRI Lucknow initiated a screening programme around 1960 in collaboration with CCNSC in USA, and is been continued at CDRI. Preliminary investigation of the anticancer activity of different plant extracts, against Ehrlich's ascites carcinoma and Schwartz Leukaemia have been carried out, 5 out of 62 plant extract showed antitumour activity. CCNSC has also started a screening programme at ICRC Mumbai. In spite of all these programmes, there are only few natural products/ drugs against cancer, that are developed in India. So it becomes necessary to have more research on medicinal plants.