Introduction
1. INTRODUCTION

After the heart diseases, cancer is the most common cause of deaths all over the world (Bernanier, 2002). Ten million new cases of cancer are diagnosed every year all over the world, half of these cases are from developing countries (National Cancer Registry Programme, ICMR, 2001). In spite of this, we have not yet being able to understand and to fully control the development of cancer.

Cancer could be defined as a malignant mass of cells with an uncontrolled and autonomous proliferative activity, and with the properties of invasiveness and metastasis to distant sites (Tanaka, 1994). Cancer cells are not the ones causing death, but the obstruction of main organs due to the uncontrolled growth of these cells. Our limited understanding of this disease may be due to the complexity of its genesis and development. Cancer is known to be multifactorial (with many different causes: biological, chemical and physical ones), multigenic (a number of genes are involved) and a multistep process (initiation, promotion and progression). Cancer patterns vary not only throughout the world but also between different population groups within the same country (National Cancer Registry Programme, ICMR, 2001), which shows the importance of geographical aspects in the origin of cancer (radiation, humidity, etc.) as well as life styles (diet, hygiene, jobs, etc.).

The most common cancer sites world wide for both the sexes are: lung, stomach, liver, colon/rectum and breast. Among females: breast, lung, stomach, colon/rectum, cervix uteri (Shibuya et al, 2002). In the case of cervical cancer, which is the number five world wide among females, there is an enormous difference in the incidence in the incidence in developed and in developing countries, 470,606 new cases of cervical cancer were registered world wide in the year 2000, out of these 91,451 (20%) appeared in more developed countries and 379,153 (80%) cases in less developed countries. The highest Age Adjusted Rate (AAR) of cervical cancer has been seen in Africans of Harare, in Zimbabwe and in Trujillo (Peru) (GLOBOCAN 2001). Worldwide geographical distribution of cervical cancer could be seen in figure 1.1. The AAR of cancer of cervix in India ranks on the higher side and is above that seen in developed countries. However, the overall AAR of all sites of cancer in females is lower than the above
Highest incidence
Very high incidence
High incidence
Low incidence

Fig 1.1: Worldwide geographical distribution of Cervical Cancer (Continued...)
Worldwide geographical distribution of Cervical Cancer

The highest incidence..............................North-East Brazil
                                   Colombia

Very high incidence.............................Central and South Africa
                                   South Asia
                                   Central and South America

High incidence....................................New Zealand (Maori population)
                                   East Germany
                                   Romania
                                   Singapore
                                   Hong Kong

Low incidence.....................................New Zealand (non-Maori population)
                                   Nigeria
                                   Zimbabwe
                                   Japan
                                   Israel
                                   Switzerland
mentioned countries (National Cancer Registry Programme, ICMR, 2001). In India, cervical cancer is the most common cancer among women. It ranks the number one among females in Bangalore, Barshi, Bhopal and Chennai. It is the number two in Delhi and Mumbai, preceded by breast cancer. Chennai had the highest AAR of 30.7 per 100,000 (National Cancer Registry Programme, ICMR, 2001). Table 1.1 shows percentage and AAR of cervical cancer in six areas of India for the years 1990-1996. Figure 1.2 depicts ten leading sites of cancer in females. It could be seen that the cervical cancer is one of the most common among the women folk in India.

Research is being carried out in many different fronts at the same time, but there is no doubt that without leaving aside the search for an efficient therapy, it would be more desirable to find the ways to prevent it. Here arises the importance of chemoprevention. It is a pharmacological intervention with natural or synthetic chemicals to prevent, inhibit or reverse the process of carcinogenesis. More than 600 potential chemopreventive agents have been identified (Tanaka, 1994), some of them can be given in diet. “Dietary cancer prevention” is understood as the changes in food consumption patterns necessary to decrease cancer development (Schatzkin and Kelloff, 1995; Goodman et al, 1997). There has been considerable scientific evidence, both epidemiological and experimental, accumulated in the past three decades, indicating that modification in diet can have a significant influence on the risk for numerous cancers (Mathers, 2003; Key et al, 2004). Of particular relevance is the consistent cancer protective effect reported for individuals consuming increased quantities of fruits and vegetables compared with those with low intakes. The past decade has witnessed a tremendous resurgence in the interest and use of medicinal plant products, specially in North America. Surveys in the American public has shown an increased usage of medicinal plants from just about 3% of the population in 1991 to over 37% in 1998 (Brevoort, 1998). The cancer inhibitory action by a variety of humans nutrients derived from plants as well as of non nutritive plant-derived constituents (phytochemicals) has been confirmed in different animal tumor models (Dragsted et al, 1993; Pezzuto, 1996) and has led to an increased emphasis on cancer prevention strategies in which these dietary factors are utilized. Lately there is also a lot of interest in “nutraceuticals” (or functional foods) with phytochemicals as constituents which have a long-term health promoting or medicinal qualities. Although the distinction between medicinal plants and nutraceuticals can sometimes
Table 1.1: Percentage and AAR of cervical cancer in six areas of India

<table>
<thead>
<tr>
<th>Area</th>
<th>Percentage</th>
<th>AAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangalore</td>
<td>21.5</td>
<td>26.1</td>
</tr>
<tr>
<td>Barshi</td>
<td>50.7</td>
<td>29.3</td>
</tr>
<tr>
<td>Bhopal</td>
<td>23.9</td>
<td>21.7</td>
</tr>
<tr>
<td>Chennai</td>
<td>26.9</td>
<td>30.7</td>
</tr>
<tr>
<td>Delhi</td>
<td>19.9</td>
<td>26.6</td>
</tr>
<tr>
<td>Mumbai</td>
<td>15.2</td>
<td>17.2</td>
</tr>
</tbody>
</table>

AAR: Age Adjusted Rate; Source: National Cancer Registry Programme 1990-1996, ICMR
Fig 1.2: Ten leading sites of cancer - Females
(Source: National Cancer Registry Programme, 1994-1998. ICMR)
be vague, a primary characteristic of the later is that nutraceuticals have a nutritional role in the diet and the benefits to health may arise from long-term use as food, i.e. as chemoprevention (Korver, 1998).

With this backdrop, in the present study, we have tested the chemopreventive potential of following six plants on cervical cancer in murine model system.

i) \textit{Trigonella foenum-graecum} (fenugreek, methi)

ii) \textit{Brassica} sp. (mustard seeds)

iii) \textit{Cuminum cyminum} (cumin, geera)

iv) \textit{Piper longum} (a variety of pepper, pipli)

v) \textit{Camellia sinensis} (green tea)

vi) \textit{Glycine max} (soybean)

The first four plants (\textit{Trigonella foenum-graecum}, \textit{Brassica} sp, \textit{Cuminum cyminum}, \textit{Piper longum}) are commonly used in Indian Culinary Art and it would be desirable to know their chemopreventive effect on cervical cancer. The last two plants (\textit{Camellia sinensis} and \textit{Glycine max}) have been chosen as the abundant literature supporting their chemopreventive effect against cancer in other sites available, and we found interesting to study their chemopreventive effect on the uterine cervix.

The importance of the present work stands not only in preventing the cancer of major death causative effect among women in India and the fifth one world wide, but also the fertility safeguard of many women who, in the case of being submitted to hysterectomy (often therapy used to cure cervical cancer when diagnosed in its first stages) would lose their fertility.