CHAPTER I
INTRODUCTION

There are approximately 600,000 plant species existing on the earth, but only a few of them have been specifically investigated chemically or pharmacologically (Wagner and Wolff, 1977). Natural drug products many of which are derived from higher plants, play an important role as useful investigative tools in pharmacological studies—morphine and codeine as centrally acting skeletal muscle relaxant, sparteine and ergot as uterine stimulant, reserpine as antihypertensive, quinine as antimalarial, essential oils and their derived terpenes as perfumes and flavoring agents and phorbol myristate acetate as a cocarcinogen.

A large part of the population in India depends even at the present time on the Indian systems of medicine, Ayurveda, Unani and Siddha. It was estimated by Chopra (1933) that about 2300 plants were used in traditional medicine practiced in the various regions of the country. Many preparations are used for fertility regulation and to induce/promote/inhibit lactation. Many of these medicines among other things contain alkaloids and steroids. While resperpine increases prolactin secretion (Lu et al., 1970) ergot derivatives such as bromocriptine have been shown to be potent prolactin inhibitors (Floss et al., 1973; Rolland et al., 1975). Winterhoff et al. (1982) have shown that extract of Lithospermum officinale has the properties to suppress thyroid
stimulating hormone and prolactin.

Breast is an end organ whose normal functioning depends upon the interactions of various hormones involved in the reproductive processes as well as general metabolism of the body. The ultimate function of the mammary epithelium is to produce milk, a unique secretion containing some substances that are synthesized by this tissue. In its progression from the embryonic to the lactating state, the epithelium proliferates along characteristic morphogenetic patterns. Mammo genesis or definitive mammary growth is one of the few developmental processes to take place in the adult animal. It is initiated at the puberty by the rising levels of ovarian steroids that stimulate the expansion of a system of branching ducts to fill the mammary fat pad (Neville, 1987). Such growth is discontinuous during ontogeny, occurring in discrete phases that are a function of the physiological state of the animal.

Breast tissue is highly responsive to the steroid and peptide hormones and there is increasing evidence that both the epithelial and stromal components can actively accumulate and metabolize hormones. Hyperplasia, secretory differentiation and involution of the breast epithelial cells occur regularly throughout reproductive life and the periodicity of these processes is controlled by changing hormonal information.

The complex hormonal milieu of pregnancy induces development of lobuloalveolar structures, the cells become more
differential and synthesize limited amounts of milk components. The high plasma levels of progesterone holds secretion in check until parturition, when an abrupt decrease in this hormone in the presence of moderate to high levels of prolactin brings about final differentiation of the gland and the onset of milk secretion. This process has been termed as lactogenesis (Topper and Freeman, 1980; Neville, 1983; 1987). Disturbance in the hormonal milieu would change the structural and functional status of the mammary epithelial cells and can also facilitate the transformation of epithelial cells leading to the tumor formation.

In the present study plant alkaloids (arecoline, vasicine and caffeine), steroid (diosgenin) and extracts (betel nut and Asparagus) which either form part of the food intake or are considered for their medicinal properties have been chosen to see their effects on the murine mammary epithelium under appropriate hormonal treatments and at different stages of development. These products have been shown to have effect on a number of biological processes. Arecoline has been reported to facilitate memory in human and other animals under certain conditions (Sitaram et al., 1978), block diurnal surge of prolactin under certain conditions (Subramanian and Gala, 1977) and have genotoxic effects (Sinha and Rao, 1985). Vasicine has shown oxytocic properties (Atal, 1980). Caffeine has a profound effect on physiological and biochemical processes including effect on neuroendocrine system, where
it inhibits thyroid stimulating hormone and growth hormone (Spindel et al., 1980, 1983). Diosgenin effects cholesterol metabolism (Cayen et al., 1979). Betel nut has been reported to have teratogenic and carcinogenic potentials (Sinha, 1984, Thesis) and Asparagus to effect milk secretion (Sabnis et al., 1968) and reduce mammary tumor incidence (Rao, 1981). Though these compounds have been studied for their effects on various organs including their effects on central nervous system, except for Asparagus, their effects on mammary gland, which could be their likely target tissue have not been elucidated. The present plan of work is precisely aimed at studying their effects on the structural and functional status of the mammary gland using mouse as the model system.