CHAPTER -1

INTRODUCTION
The Reproductive health of women is an emerging concern in the present society. The concern has been raised with the concept of pregnancy control but with better "Reproductive Health". With many other serious health issues of women, the ill reproductive health burdens with death of many women in each year (high mortality rate of women) due to complications in pregnancy, child birth and abortion. India accounts a high maternal mortality ratio of approximately 453 deaths per 100,000 births in 1993 (Velkoff and Adlakha, 1998). Therefore, over the last few years, the health councils, research organization, social activist groups and policy makers have been giving much emphasis on women reproductive health for safe motherhood as well as prevention and solution of reproductive health problems. The World Health Organization (WHO) considers the reproductive health as the primary health care services made available to ensure the well being of female physical health encompassing the issues like fertility, infertility, contraception, safe motherhood, minimization of the complications of the abortions and managing its consequences safely and humanely, health care for beyond or during the childbearing age of women as well as other needs of men. In 1990, the U.S. government has established the U.S. National Institutes of Health, an office, for research on women’s health and recently launched a ten year women’s health initiative (Edited by Harrison et al., 1996a). The Cairo International Conference on Population and Development (ICPD) held in September 1994 emphasized on the elimination of social and economic discrimination against women, promoting economic growth and achieving sound population policies. In this conference the dignitaries all over the world shifted their ideas of population control merely from demographic to the quality-of-life imperative (Egon Diczfalusy, 2000).

All these have boosted a ‘women centered’ approach in Reproduction regulation and/or control research and development. At the same time with the technological
advances the introduction and uses of oral contraceptives and other contraceptive devices has fulfilled the needs of individual to a great extent for fertility regulation. However, currently available contraceptives fall short of meeting the requirements in view of the changing structure of contraceptive needs. There are still around 238 million women worldwide who are at the risk of unwanted pregnancy, because of their non access to contraception, sometimes misuse and/or due to contraceptive failure (Guttmacher Institute, 1995). A report of United Nations Population Fund says there are still around 350 million women worldwide who lack access to modern contraceptive methods (United Nations Population Fund, 1997). While there are around 80 million pregnancies are unwanted each year, 34 million women gave unintended births and 42 million pregnancies that women decide to resolve in abortion (Speidel et al., 2008). Around one third of the 190 million pregnancies in the world in 1995 ended in abortion (Edited by Harrison et al., 1996b). However, the number of induced abortions declined world wide between 1995 and 2003, from nearly 46 million to approximately 42 million (www.guttmacher.org). Clearly, of the millions of unwanted pregnancies that ended in abortion, a high number of such abortions are performed in unsafe and illegal way. Many a time some social issues compel to terminate many pregnancies in unsafe and septic conditions and in illegal ways. In developing countries more than 500,000 maternal deaths that occur annually is because of unsafe abortions (Edited by Harrison et al., 1996b). Such Social taboo and psychological distress of women raise the need of development of drugs and methods that will work in post implantation period or as a safe abortifacient medicine. When many hormonal drugs have been used as oral contraceptives, scientists are yet to develop a safe drug for abortion or as post implantation alternative.

Moreover, to reduce the excess steroid exposure and to lessen the side effects, a non steroidal drug is the need of the hour for better reproductive health. The WHO has set
up a task force to explore a nonsteroidal drug of herbal origin all over the world (Griffin, 1988). The aim was to explore the traditional medicine prevails among different communities. WHO introduced the first global strategy for traditional and complementary alternate medicine (TAM and CAM) within the year 2005 (ISIS report 1st August, 2002). The WHO also intends to integrate the TM in to the "National Health system globally".

The use of herbs as a natural source of food and healthcare is not new for the mankind. Variance in the abundances and availability of plant species from zone to zone has developed the practice of using the herbs available locally for their (mankind) various need. This practice has developed the tradition of using herbs for healthcare and with the passage of time establishes own traditional and indigenous knowledge system of different communities. The use of Traditional Medicine (TM) still prevails in many parts of the world and developing new alternate drugs from traditional system is a world wide interest. TM has maintained its popularity in many Asian countries including India and China. WHO survey says around 80% of the population living in the developing countries still relies almost exclusively on TM for their primary healthcare needs (Reviewed by Goyal et al., 2007). Our own country India itself is rich with its oldest known healthcare systems of Ayurveda, Unani and Sidha. There are about 45,000 plant species in India, including 3000 officially documented plants with medicinal potential (Reviewed by Seth and Sharma, 2004). In rural India, 70 % of the population is still dependent on the traditional system of medicine the Ayurveda (Reviewed by Bent et al., 2004). Ancient Indian literature abounds with the records of using a large number of plant species for contraceptive and abortifacient properties. Ayurvedic texts mentioned the traditional use of *Hibiscus rosa sinensis*, *Avrodhak (Lawsonia inermis)*, *Embelia ribes*, *Adhatoda vasica* and many other plants as a fertility regulator. For development of this system scientifically, the Government of India also has set up a multidisciplinary interdepartmental task force
coordinated by council of research in *Ayurveda* and *Sidha* to develop herbal contraceptive. The planning commission with an objective to protect India’s medicinal plant resources and traditional knowledge has set up a task force on conservation and sustainable use of medicinal plant in the year 2000. Under this mission 90 medicinal plants have been decided to conserve on a priority basis and to set up a traditional knowledge digital library (TKDL) to protect India’s ancient knowledge (Choudhury *et al.*, 2000).

The north east India, being a biodiversity hotspot is rich of its flora and fauna. The indigenous people of this region have an age old tradition of using herbal preparations for curing and prevention of diseases. Many of such herbal preparations are also known to use for prevention of unwanted pregnancies by the indigenous women. In the present research work, one of such herbal preparations made from the stem bark of plant *Dysoxylum alliarium* has been investigated for its antireproductive property especially during peri implantation period in rats. The first hand knowledge of the present investigator revealed that the indigenous women of ‘Adi’ tribe in Arunachal Pradesh use the crude bark powder of this plant to terminate the pregnancies of their domestic pets (dogs and pigs) and often for women’s unintended pregnancies. The local people fed the bark powder with fodder to the female pets during the post coital period to avoid growth of the population of the animals. Important to note that, the crude bark powder is fed to only known mated females to avoid give birth of pups. Following this oral folk literature information and observation, the crude bark powder of the plant (*Dysoxylum alliarium*) has been tested for its post-coital antireproductive property and for its use as an abortifacient medicine. Initially, the crude bark extract was subjected to thin layered chromatographic fractionation to understand the chemical nature of active compound. The histological studies of the ovary and uterus of normal cyclic female and pregnant rats have been done to observe the effect of the crude bark powder on the targeted reproductive organs (ovary
and uterus) during the pre and periimplantation period. To study the changes in the uterine protein (growth factor) profile during the post implantation period the endometrial protein were separated by SDS-PAGE. Before the work carried out, it was hypothesized that the pregnancy hindering effect of the bark of *Dysoxylum alliarium* may be due to it’s adverse effect on certain uterine growth factor, which participation during the embryo-uterine attachment event of post implantation period might be very crucial. Vascular Endothelial Growth Factor (VEGF), a potent growth factor for the angiogenesis and embryonic blood vessel formation during periimplantation period had been selected to study its (VEGF) expression level during the drug treated period. Consequently, the western blotting studies and immunohistological studies of uterine section had been done to investigate any changes in the VEGF expression as a result of herbal drug treatment. Study of toxicity is an important parameter for a traditional health friendly medicine. Therefore, toxicological evaluation of the tested herbal drug (crude bark powder of *Dysoxylum alliarum*) has also been done. The toxicity of the crude extract was tested by studying the level of the two hepatic enzymes Serum glutamic oxaloacetic transaminase (SGOT) also known as aspartate aminotransferase (AST) and Serum glutamic pyruvate transaminase (SGPT) known as alanine aminotransferase (ALT) spectrophotometrically during gestation. Histological studies of liver tissues has been carried out following long term treatment (day 1–15 of gestation) treatment of CBP during gestation.

The overall content of the thesis has been written in six chapters. A brief introduction on the relevance of the present research topic in the context of Indian national and International values has been presented in the first chapter. During the last few decades increasing numbers of research articles on the use of natural products as reproduction regulator has been published world wide. A brief review of pertinent literatures of the resent research topic has been incorporated in the chapter-2. The
materials and methods followed for the present work has been described in the third chapter. This section covers the experimental design, collection of plant materials, its extract preparation and administration to female cyclic non pregnant and pregnant rats and initial fractionation of crude extract by thin layer chromatography (TLC). Parameters like study of implantation sites, histological observation of ovary and uterus, separation of endometrial protein, western blotting and immunohistochemical studies of VEGF, enzyme studies for toxicity and method of statistical analysis have been mentioned under this chapter. Results of the experiments have been presented in the fourth chapter. The experimental findings of the thin layer chromatographic separation of the crude extract, implantation study, histological findings of the ovary and uterus, separation of the uterine protein by SDS-PAGE, VEGF studies by western blotting and immunohistochemistry and toxicological evaluations have been described with relevant figures and tables in this chapter. The discussion of the experimental findings has been included in the fifth chapter. The data obtained from the results were analyzed and discussed with relevant references in the discussion chapter. In the sixth chapter, glimpses of the whole research work have been placed as summary and conclusion. Lastly all the relevant references to the present work are presented in the form of Bibliography.

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