Abstract
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Cancer is a multifactorial, multifaceted, and multimechanistic disease requiring a multidimensional approach for its treatment, control, and prevention. Cancer involves fundamental biological progress concerning disorganized cell replication, cell death and disorganization of organ structure. It is a class of diseases or disorders characterized by uncontrollable of cells and the ability of these cells to invade other tissues, either by direct growth implantation into distant sites by metastasis. It may affect people at all ages, but risk tends to increase with age, due to fast that DNA and it is one of the principal cause of death in developed countries.

In India, roughly a million people die annually of cancer. The incidence of cancer is on the rise, with multiple risk factors that involve interplay between genetic and environmental components. Diet is a major environmental risk factor. The contribution of diet and nutrition status to cancer risk and conversely to the prevention and treatment of cancer has been a major focus of research as well as public health policy.

However, nature was not creating antibiotics for cancer. It is generally treated by Surgery, Chemotherapy, Radiation therapy, immunotherapy, or other methods. Most anticancer drugs act by damaging the DNA with in cancer cells, inhibiting their ability to proliferate unfortunately, these drugs also damage the DNA of normal cells and thereby produce several side effect. In contrast, chemopreventive natural agents have low side effects and toxicity, neutralization of carcinogenesis as well as their effects on cells.

Medicinal herbs constitute an important source for traditional systems of medicines (Ayurveda, Homoeopathy Siddha, Chinese medicine and Herbalism) and plant extracted system of medicines.

Today pharmaceutical companies are extensively researching rain-forest plants materials for their medicinal potential, as herbs remain the foundation for a
large amount of commercial medications used today for treatment of Cancer. Cancer research is the intense scientific effort to understand disease processes and discover possible therapies.

Thus, R&D thrust in the pharmaceutical sector is focused on development of new drugs, innovative / indigenous processes for known drugs and development- of plant based drugs through investigation of leads from traditional systems of medicine. Traditional knowledge will serve as a powerful search engine and most importantly; will greatly facilitate intentional focused and safe natural products research to rediscover the drug discovery process.

The future of natural products drug discovery will be hare holistic, personalized and involve wise use of ancient and modern therapeutic skills in a complementary manner so that maximum benefits can be secured to the community.

The world Health Organization (WHO) also has recognized the importance of traditional medicine and has been active in creating strategies, guidelines and standards for Natural medicine, example of plant derived medicines and its pharmaceutical formulation are vinblastine (velban®), vincristine, (leurocristine, oneovin®). Paclitaxel (Taxol®), camptothecin, podophyllotoxin. Many molecules obtained from nature have shown wonders, there are a huge number of molecules that still remains either to be trapped or studied in detail by the medicinal chemists. The present thesis entitled “Bioinorganic and electrochemical analysis of some anticancer natural drugs and pharmaceutical formulations” reports the Analysis of drugs and its pharmacological formulations using Modern organic electrochemical technique with its proposed electrochemical mechanism. The Thesis also reports the ligation aspects of these drug with certain life essential metal ions and biological testing (antimicrobial and In-vitro Activity) of the complexes understudy has also been mentioned.
Abstract

The thesis has been discussed in three chapters -

Chapter – 1

The first chapter of the thesis opens with an introduction to cancer, its nature type, and various types of cancer treatments. The chapter also includes importance of Natural chemo preventive agent in the treatment of cancer. The bioinorganic study of drugs (metal-drug complexes) has been discussed in details. A reasonable introduction to the organic electrochemical techniques and their application for the characterization of metal drug complexes has also been mentioned. A brief introduction to antimicrobial and pharmacological studies on metal drug complexes has been reported. Besides aim and scope of the work has been mentioned.

Chapter – 2

This chapter has been divided into two parts. Chapter 2(A) and chapter 2(B). In Chapter 2(A), an up to date survey of relevant literature as regards to the problem under taken has been reported. Chapter 2(B) reports the experimental details of the work undertaken. It describes about the different procedures for the present study particularly regarding the polarographic study of the metal ligand complexation equilibrium, amperometric titrations, and IR studies on the prepared complexes.Besides, details regarding the biological studies on metal-drug complexes have been mentioned.

Chapter – 3

Chapter 3 incorporates results and discussion part of the thesis. The chapter has been divided into four parts i.e. chapter 3(A) 3(B) 3(C) and 3(D).

Chapter 3(A) deals with the study of Anticancer Drugs Curcumin, Beta-carotene, Aloe-emodin (AE), and Indole-3carbinol (13C) in extracted sample from plants
and pharmaceutical formulations. This chapter also reports the possible electrochemical behavior of the above compounds (drugs) in different environments. Example curcumin (yellow pigment extracted from Turmeric) shows two conjugated peaks by using differential pulse polargraphy (DPP) at pH 8.1± 0., and its Ep value is –1125 mv and –1275 mv Vs SCE. However, the DCP (Direct current polarography) show only one polarographic wave with E1/2 = -1275 mv Vs SCE in Ammonium tartrate as supporting electrolyte. Curcumin is involved in two electron reduction process at pH 8.1± 0.1. The two double bonds which are by the side of the OH and C=O groups are reduced to give a doublet by using differential pulse polargraphy (DPP).

Chapter 3(B) includes bioinorganic study of curcumin, I3C (Indole-3 carbinol), AE (Aloe-emodin) and Beta-carotene. Bioinorganic chemistry is specialized field that spans the chemistry of metal containing molecules with-in biological system. However, organisms require a number of other elements to carry out their basic functions. Many of these elements are present as metal ions that are involved in crucial biological processes such as respiration, metabolism cell division, muscle contraction, nerve impulse transmission and gene regulation. As such, life essential metal -drugs complexes have been prepared as modified forms of the extracted active principle e.g. Fe (II) - Complexes with all the four anticancer drugs understudy. The results of polarographic study revealed 1:1 metal:ligand ratio for Fe(II)- curcumin, Fe(II)- Beta carotene, Fe(II)- Aloe-emodin and Fe(II)-Indole-3carbinol complexes. The results of amperometric, study also confirmed above observation. IR studies on complexes clearly confirm the binding site of metal with parent drugs (ligand) for example curcumin binds with Fe (II) through its carbonyl group. Biological study was done by using Anti-microbial, Antifungal and in-vitro pharmacological studies. Results of Anti-microbial studies and antifungal studies show that metal complexes posses' higher toxicity in
comparison to the parent drug against some gram-negative gram-positive bacteria and fungi. Data of In-vitro pharmacological study show that all the complexes were more effective than parent drug against cancer cells (In-vitro). The In-vitro activity was performed against HELA Cancer Cells.

Chapter 3 (C) discusses the results of polarographic, amperometric and spectrophotometric analysis on the Cu (II) complexes with all the four drugs under study. The results showed 1:1 ratio for Cu (II) complexes with curcumin, Indole-3-carbinol, beta carotene and Aloe-emodin. Which are similar to that discussed earlier. The results of antimicrobial studies on the complexes understudy revealed that all the complexes possess toxic response against test pathogens, except for Cu(II) - Aloe emodin against, Fusarium oxysporum Fungi. Increased anticancer activity has been observed with Cu(II) complexes of all the four drugs understudy. In vitro study of Cu (II)-aloe-emodin complex is shown that the anticancer behavior is less than the parent drug but other complexes show more toxicity against HELA cancer cells.

Chapter 3 (D) deals with the results of polarographic, amperometric and IR studies on Zn(II). Complexes with the above drugs which state that complexation ratio for Zn (II)- curcumin Zn(II) Beta carotene, Zn(II)- Aloeemodin of 1:1 and it is 1:2 for Zn(II) Indole-3-carbinol. IR studies on the Zn(II)-complexes with all the four anticancer drugs confirmed the involvement of different group in complex formation process. Results of antimicrobial study on the complexes understudy show that all the complexes show reasonable toxic affect against pathogenic bacteria understudy. In vitro study of Zn (II)-13C (Indole-3-carbinol) complex is shown that the anticancer behavior is higher than the parent drug but other complexes show more toxicity against HELA cancer cells.
Conclusion

On the basis of above studies conclusion has been drawn that in general the Analytical methods, which I have used for my present research, are simple and less time consuming and the developed methods have a great importance in the Analysis of drugs obtain from different environments. polarography showed remarkable ability to adjust to ever increasing demands on the sensitivity and selectivity and up to now mercury electrodes are among the best sensors for electroanalytical measurements. Results also confirm that complexes are found to be more effective as regards to their chemo preventive activity as compared to the respective parent drug. As such, they may be recommended to the therapeutic experts to decide over their possible use in cancer therapy.