



Comprehensive Review on the “Liquorice as an Anticancer aid.”

Miss.Misal Pooja Rajaram¹,Mrs.Bhongale Priyanka A.²

YSPM's Yashoda Technical Campus Faculty of Pharmacy,Wadhe,Satara.

Corresponding Author E-mail: poojamisal2511@gmail.com

ABSTRACT-

One of the greatest health problems facing humanity is cancer, a terrifying illness that necessitates an aggressive treatment plan. Plants offer a promising avenue for cancer research since they are reservoirs for novel chemical entities. Chemotherapy has been beneficial thus far, but it also comes with some quite unpleasant side effects. Plants and plant-derived products, however, are an area that is revolutionizing itself because they are less poisonous, quicker, cheaper, safer, and more environmentally friendly than traditional treatment approaches. The actions of phytochemicals are targeted tumour cells only, sparing healthy cells from harm. The process of carcinogenesis is intricate and involves numerous signalling pathways. Since phytochemicals have pleiotropic effects on target events in various ways, they are thought to be good candidates for the creation of anticancer drugs.

Research is currently being conducted to identify possible candidates from these phytochemicals that have a tendency to prevent or inhibit the proliferation of cancer cells without causing adverse effects. A number of phytochemicals and the analogues they produced have been found to represent promising options for anticancer treatment. Through this thorough study, efforts have been made to draw attention to the most recent advancements and significant achievements in Phyto molecules based cancer therapeutics that target nuclear and cellular components.

Introduction –

At present, the concept of health consciousness in urban and rural people is becoming increasingly popularized. Keeping in mind the health effects of modern medicine, people have been using herbal medicines either alone or in combination with other products to achieve this state of health. There are substantial monetary profits associated with the expansion and use of plants with medicinal importance and their associated products in aboriginal medications in disease treatment, which indicates that the ways are widening for the herbal renaissance. This is evident from reports published by the World Health Organization (WHO) that 70%–80% of the global population fulfil its primary healthcare needs by using different herbs for medicinal purposes. From prehistoric times to present day, about 53,000 species of herbs are exploited in human treatment. The controlled accessibility of various agents needs to be considered if plant-based medicinal products are to be developed as chemotherapeutic medicines. Due to this overexploitation, many species are threatened with extinction. For the judicious use of herbal medicines and their products, great should be care kept in mind while using these herbal medicines, and their overexploitation must be controlled. This can only be achieved when we strive hard to implement three major goals of the Convention on Biological Diversity (1992): conservation of biodiversity, sustainable use of biodiversity components, and fair and equitable benefit sharing from genetic resources.through the plants possessing medicinal and aromatic properties play a significant role in treating various ailments, herbal therapy has been Throughout the years, it has been widely utilized to treat, prevent, and promote health as well as to increase life expectancy and quality. Nevertheless, a systematic assessment of their efficacy and safety is lacking. Herbal medicine appeals to many due to its holistic approach to health care, but the large number of variables that need to be included in its scientific evaluation also makes it extremely difficult to evaluate. Herbal medications are widely used, and while many people think they are safe, they are frequently combined and derived from plant sources, which vary widely in terms of species, growing environments, and physiologically active ingredients.

Since the beginning of human history, people have used plants, herbs, and botanicals in order to encourage health and treat illness all across the world. The foundation of contemporary medicine is derived from plants and other natural sources, which also play a significant role in the production of commercial medicinal compositions. Plants are the source of about 25% of medications that are given globally. Herbs are still frequently utilized in medicine instead of pharmaceuticals. Herbal medicine is the recommended treatment option for certain individuals. Herbs are utilized by some as a complementary treatment to traditional medications. But in many impoverished nations, the only accessible or reasonably priced medical system is traditional medicine, of which herbal therapy is a fundamental component. For any reason, people who take herbal remedies ought to be

Cancer-

The word "cancer" refers to a broad category of malignant diseases that can affect various internal parts. These disorders are typified by the fast and uncontrollably forming aberrant cells that can aggregate to create a growth or tumour or spread throughout the body to trigger aberrant growth at other locations. If the process continues without interruption, it can continue until the organism dies. Surgery, radiation therapy, and pharmaceuticals (cancer chemotherapeutic agents) are the primary methods of therapy for advanced stage cancer in humans. Chemotherapeutic treatments for cancer can

sometimes cure the disease as well as prolong its course and temporarily relieve its symptoms. Though they have greater adverse effects, many hundreds of chemical variations of the known class of cancer chemotherapeutic drugs have been produced. but have more adverse consequences. An effective anticancer medication should destroy or seriously damage cancer cells without damaging healthy cells. Because this goal is hard, if not impossible, to achieve, cancer patients often experience severe side effects from their treatment.

Early thoughts about Cancers

The human body is so much more understood today than it was for the early Greek physicians. According to Hippocrates, the body is made up of four fluids: black bile, yellow bile, phlegm, and blood. He thought that cancer was caused by a large number of black bile at any one location within the body. For the following 1400 years, this was the accepted theory on the cause of cancer. Three developmental stages are involved in the production of a malignant tumour in the ancient development of cancer. A DNA mutation that either undergoes improper DNA repair or no DNA repair at all makes up the initial stage of the process. The second phase, known as promotion, is taking steps to encourage the unchecked development and spread of mutant cells. In Over time, these cells cease to function normally and merely divide. Metastasis is the third stage. This includes the spread of malignant cells to neighbouring tissues and their movement through circulatory or transport systems to other tissues. When substances are added to the body, they may promote change, cause mutations, or do both. A "complete carcinogen" is a substance that causes both cancers. Tissue injury can result in the proliferation of cells. Certain mutagens can cause harm to the tissues around them, which encourages cell division. Cancer could possibly result from this.

Cancer Epidemiology:

More than 12 million new cases of cancer are predicted to emerge globally in 2007; 5.4 million of those cases are expected to occur in economically developed nations and 6.7 million in economically developing nations.

According to estimations, there will be 7.6 million cancer deaths worldwide in 2007 approximately 20,000 fatalities per day of which 2.9 million will occur in economically developed nations and 4.7 million in poor nations. Due to population growth and aging alone, the worldwide burden of cancer is predicted to increase to 27 million new cases and 17.5 million cancer deaths by 2050. The World Cancer Report is a succinct guide that details the prevalence of cancer worldwide, its causes, the main forms of cancer, early identification, and treatment options. The World Health Organization's (WHO) IARC published the 351-page worldwide study. WHO Director-General Dr. Gro Harlem Brundtland. A Global Strategy on Diet, Physical Activity, and Health is also being developed by WHO. in accordance with a mandate issued by Member States in May 2002 to address the rising worldwide burden of chronic illnesses, such as cancer, heart disease, diabetes, and obesity. In order to develop the plan, which will be presented to the World Health Assembly in May 2004, WHO is working extensively with Member States, other UN agencies, the commercial sector, and civil society. The plan will include suggestions for the government for physical activity and dietary objectives as well as population-based measures aimed at lowering the incidence of chronic illnesses like cancer.

In 2000, cancer was estimated to have caused around 7 million fatalities globally, or 12% of all deaths. The only diseases to cause more deaths than cancer were cardiovascular (30% of all deaths) and infectious and parasitic disorders (19%). In the same year, it was projected that cancer accounted for over 6% of the total worldwide disease burden. While the risk of acquiring or dying from cancer is still higher in wealthy countries, over 70% of all cancer fatalities occurred in low- and middle-income countries.

There is a growing the worldwide burden of cancer due to the control of communicable diseases and population aging in developing nations. In fact, Pisani et al. predicted that between 1990 and 2010, demographic shifts will cause a 30% increase in cancer-related fatalities in rich countries and more than twice this amount (71%), in developing countries. Malignant tumours accounted for 12% of the approximately 56 million global deaths in 2000 due to all causes. Cancer is the leading cause of death in many developing nations. A total of 6.2 million people died from the disease in 2000, with 5.3 million men and 4.7 million women suffering malignant tumours.

The research study also shows that, similar to its impact in developed countries, cancer has become a significant public health issue in developing nations. By 2020, the number of cancer cases globally could rise by 50% to 15 million. The World 4 Cancer Report offers convincing proof that infections, diet, and smoking cessation may all be prevented.

Causes Of Cancer -

It arises from one single cell. The transformation from a normal cell into a tumour cell is a multistage process, typically a progression from a precancerous lesion to malignant tumours. These changes are the result of the interaction between a person's genetic factors and three categories of external agents, including:

Physical carcinogens: such as ultraviolet and ionizing radiation ,

biological carcinogens: such as infections from certain viruses, bacteria or parasites.

Viruses: hepatitis B for liver cancer, Human Papilloma Virus (HPV) for cervical cancer, and human immunodeficiency virus (HIV) and Kaposi for sarcoma.

Bacteria: Helicobacter pylori and stomach cancer.

Parasites: schistosomiasis and bladder cancer. Bladder cancer

Arsenic; solvents; aromatic amines; petrochemicals and combustion products; metalworking fluids and mineral oils; ionising radiation. Bone cancer Ionising radiation.

Brain and other central nervous system cancers contains Lead ,arsenic and mercury. solvents including benzene, toluene, etc

Types of Cancer :**1) Cancers of Blood and Lymphatic Systems:**

- a) Hodgkin's disease
- b) leukaemia's
- c) Lymphomas
- d) Multiple myeloma
- e) Waldenstrom's disease

2) Skin Cancers:

- a) Malignant Melanoma

3) Cancers of Digestive Systems:

- a) Oesophageal cancer
- b) Stomach cancer
- c) Cancer of pancreas
- d) Liver cancer
- e) Colon and Rectal cancer
- f) Anal cancer

4) Cancers of Urinary system:

- a) Kidney cancer
- b) Bladder cancer
- c) Testis cancer
- d) Prostate cancer

5) Cancers in Women:

- a) Breast cancer
- b) Ovarian cancer

6) Miscellaneous Cancers:

- a) Brain cancer
- b) Bone cancer
- c) Characinoid cancer
- d) Nasopharyngeal cancer

Mechanism of cancer:

Chemical carcinogens are frequently digested by cells once they are internalized, and the resultant products of metabolism are either eliminated or stored by the cell. Carcinogens or the metabolic products they produce within the cell have the ability to directly or indirectly impact gene expression and regulation that is involved in cell-cycle control, DNA repair, cell differentiation, and apoptosis. Certain carcinogens cause chromosomal breakage, fusion, deletion, mis-segregation, and non-disjunction, among other genotoxic mechanisms of action. For instance, chromosome abnormalities in terms of number and structure can be brought about by carcinogenic ions or compounds containing nickel, arsenic, and cadmium. Others work by non-genotoxic means, like immunosuppression, inflammatory induction, reactive oxygen species production, activation of receptors like the oestrogen or aryl hydrocarbon receptors. When these genotoxic and nongenotoxic mechanisms work together, they can modify signal-transduction pathways, which in turn causes resistance to apoptosis, genomic instability, hypermutability, and loss of control over proliferation.

Stages of Cancer :

At the time of diagnosis, the disease's degree or transmission is described. The size, location, and extent of the initial tumour, as well as whether it has spread to other bodily parts, determine the stage of a malignancy. Tumours are categorized using a variety of staging schemes. Three factors are taken into consideration when evaluating a tumour by the TNM staging system: the size of the primary tumour (T), the presence or absence of regional lymph node involvement (N), and the presence or absence of distant metastases (M). A stage of I, II, III, or IV is assigned after the T, N, and M have been established; stage I denotes an early stage of the disease and stage IV, an advanced one. An alternative summary staging scheme (local, distant, regional, and in situ) . Invasive cancer is one in which the cancerous cells have penetrated beyond the initial layer of tissue. The staging procedure is used to determine the extent of a malignancy. Unless the cancer is very large, basal cell carcinoma is rarely staged since it rarely spreads to other organs. Staging may occasionally be necessary for squamous epithelial cell tumours due to their slightly increased (albeit still very low) chance of spreading, especially in those with a high risk of doing so. This includes HIV-positive individuals as well as transplant recipients whose immune systems are weakened by medication.

Anticancer herbal drug :

Glycyrrhiza glabra :

Basic introduction of *Glycyrrhiza glabra* (Liquorice) :

Liquorice is the well known traditional herb used for the various alignment. It is often cultivated for its edible roots, which is widely used in medicine. The plant needs deep well cultivated fertile moisture retentive soil for good root production. Also it prefers a sandy soil with abundant moisture and does not flourish in a clay. Slightly alkaline condition produce a good plant. A plant thrives in a maritime climate. It is propagated using seeds and roots. Harvesting is generally occurs in an autumn of the 4th year. The soil is carefully removed from the space between the rows.

Plant profile :

Synonym : Radix, sweet Glycyrrhizae liquorice.

Biological Source : Liquorice consist of subterranean peeled and unpeeled stolons, roots, and stems of *Glycyrrhiza glabra* Linn., belonging to family Leguminosae.

Geographical Source : It is mainly found in China, Europe, India, Iraq, Japan, Kurdistan, Spain and other united states.

Chemical Constituents – Liquorice contains more than 20 triterpenoids and nearly 300 flavonoids. Among them, glycyrrhizin (GL), 18 β -glycyrrhetic acid (GA), liquiritigenin (LTG), licochalcone A (LCA), licochalcone E (LCE) and isoliquiritin

Licochalcone A: has been shown to modulate signalling pathways involved in cancer development, such as the NF-kB pathway. forming LC-2 protein. So it contribute to its potential as a therapeutic agent against lung and colon cancer.

Isoliquiritigenin : it is a phenolic compound found in a liquorice. It exerts its chemoprotective effects by induction of cytoprotective protein and show their potential against the colon cancer.

Glycyrrhizin : it is chief constituent of liquorice root. It regulate the Nitric Oxide production and induces DNA damage and apoptosis in cancer cells by activating the apoptosis signal-Kinase -1. Also it inhibits the growth and spread of lung cancer and fibrosarcomas.

Glycyrrhetic acid : it is a triterpenoid compound derived from the liquorice root. It protects against aflatoxins, i.e. powerful fungal carcinogens in liver. and stimulates the immune response of the body and protects against colon cancer and oestrogen positive breast cancer

Liquorice Root :

Root of liquorice is a long, cylindrical, unpeeled pieces, several feet in length, varying in thickness from ¼ inch to about 1 inch. Longitudinally wrinkled, externally greyish brown, internally tawny yellow, pliable, tough, texture coarsely fibrous. It contains several of the chemical constituents which has a greater potential against the cancer.

Uses of Liquorice:

A) Antioxidant Effect :

Liquorice contains compounds with antioxidant properties, which may help protect cells from damage caused by free radicals. This oxidative stress is linked to the development of cancers. **Anti-Inflammatory Effects:** Chronic inflammation is associated with

B) Development of cancer :

Liquorice shows anti-inflammatory effects, potentially reducing the risk of cancer development.

C) Apoptosis Induction :

Apoptosis, or programmed cell death, is a natural process that helps regulate cell growth. Glycyrrhizin may induce apoptosis in certain cancer cells, leading to their destruction.

D) Inhibition of Angiogenesis :

Angiogenesis is the formation of new blood vessels, a process crucial for tumour growth. Some research suggests that liquorice compounds may inhibit angiogenesis, potentially limiting the blood supply to tumours.

E) Immune Modulation :

Liquorice may have immune-modulating effects, influencing the activity of immune cells. This could potentially enhance the body's ability to recognize and eliminate.

Liquorice Herbal Formulation –

1. *Glycerrizin liquid formulation*

Ingredients :

Liquorice powder extract
Phosphate buffer solution
Glycerine and polyethylene glycol (55:5)

Procedure :

Glycerrizin (Liquorice powder) was dissolved with aqueous or non aqueous solvent.i.e 400mm phosphate buffer solution having PH 7.0. then add glycerine and polyethylene glycol 400/PG ratio 55 : 5 mix well. by hot plate stirrer for 30-120 min. at temperature 60 degree.to make formulation.

2. *Liquorice antioxidant cream :*

Ingredients :

Liquorice root extract (Glycyrrhiza glabra)
kojic acid, steric acid .
0.1M Phosphate buffer solution.
Propylene glycol

Procedure:

500gm of liquorice powder was macerated at 4 hrs. by using 5 lit. Ethanol. And filtrate is evaporated in a rotary evaporator to obtain ethanolic liquorice root extract.

Mix the oil phase (steric acid,acetyl alcohol),add liquorice extractAdd 0.1M phosphate buffer solution having PH 6.8. add aqu. Phase (polyethylene glycol) . and heated at 70-75 degree Celsius.

3.*Traditional drink of Hibiscus and liquorice :*

The plant materials hibiscus and liquorice were dried in an oven at 50±1°C then powdered using a lab grinder and stored in air- tight jars maintained at 4°C till use. Dried materials (10g) were extracted with distilled water by soaking at room temperature for 48 hr. The extract was centrifuged at 2000 rpm for 15 min. Extraction and filtration were repeated until the residue was colourless. The solvent was removed under vacuum at 40oC using a rotary evaporator . Extracts were freeze-dried using lyophilizer. The obtained powder were kept in light- protected containers at -18oC until further it used as a traditional drink for treat cancer. It induces apoptosis and treat breast cancers.

Conclusion:

drugs derived from chemicals have been developed to treat secondary tumours. Therefore, several of the existing methods, like chemotherapy, have limitations due to their harmful effects on non-targeted tissues, which can lead to medical problems in humans. Consequently, there is a demand for complementary therapies that contain anticancer drugs obtained from plants, with plants being the best source. People's health has improved through the use of medicinal plants. Important facts about plant extricates and the bioactive substances they contain that have an anticancer effect must be examined for. Plant-based drugs have been developed as a result of promising research findings and have progressed to clinical trials.

People's health has become better through the use of medicinal plants. Important facts about plant extricates and the bioactive substances they contain that have an anticancer effect must be examined for. Plant-based drugs have been developed as a result of significant investigations and have reached the preliminary stages of clinical trials. Liquorice-based medications have strong anticancer properties. These substances are easily obtainable from the typical environment and have a somewhat non-toxic effect on healthy human cells. Strong inhibitors of cancer cell lines make plant-derived anticancer specialists desirable .It is important to learn how to be mindful of demands and reasonable when using these agents, as misuse can occur. This review assisted others in their exploration by providing a list of plants that exhibit anticancer efficacy against different forms of cancer.

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