

CHEMICAL ASPECTS AND ROLE OF PHYTOMEDICINES AS POTENT ANTI-CANCER DRUGS

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ABSTRACT

Cancer is one of the fatal diseases which results in millions of deaths every year. Annual mortality rate tremendously increased with the increase in cancer worldwide. Several anticancer drugs have been synthesized but they are very expensive. Also, the number of these drugs is not satisfactorily meeting the time requirements. Furthermore, the synthesis of these drugs in laboratory is an expensive and laborious process, therefore, there is a need to extract these drugs from medicinal plants. Phytochemicals or naturally occurring plant compounds are important sources for new medications and are also used to treat cancer. This review focuses on the families of some plants with chemicals that can inhibit cancers at different stages. These chemicals might be used as potent anti-cancer drugs because of their ability to prevent tumours.

Keywords: Medicinal Plants, Herbal drug, Phytomedicines, Anticancer herbs, Anticancer drugs,

INTRODUCTION

It is believed that healthcare with by the utilization of plants possessing the medicinal applications is being used since the time of the creation of life on earth. Research has been carried out and a huge data have been published globally which verify the efficacy of plantbased

medicines. Findings of these studies also proven helpful to produce such medicines. Exceeding a value of \$100 billion per annum shows the importance of medicinal plant products globally. This review discusses the contribution and applications of medicinal plants in prevention and treatment of various types of cancer, by extraction of various useful chemicals from plants for the measurement of inhibition effect of these extracted drugs. The importance of plants possessing medicinal applications against the prevention of various diseases is further investigated under core and leading principles described by primary health care (PHC) approach. (Berglund & Lindmark, 2016; Mlilo & Sibanda, 2022; Rankoana, 2022; Sofowora, Ogunbodede, Onayade, & medicines, 2013)

Herbs are very important plants as they have been used as bases of medicines. Their role against many viral, fungal, and bacterial diseases, and their immune stimulating characteristics make them an important agent against the treatment of various fatal diseases. This immune stimulating property makes them potent anti-cancer agent which diminishes the risk of various cancers. A huge number of phytochemicals which include terpenoids, flavonoids, lignans, sulphides, polyphenolics, curcumins, carotenoids, saponins, phthalides and plant sterols have been identified in these herbaceous plants. Most of the herbaceous plants possess anti-toxicant compounds, which might be proven helpful against chronic diseases. Their defence against LDL cholesterol from oxidation results in the inhibition of lipoxygenase and cyclooxygenase enzymes which is considered to prevent lipid peroxidation or possess antitumor activity (Khodadadi, 2015).

What is a medicinal plant?

A plant which has one or more organs containing substance which may be used for therapeutic purposes is referred to as a medicinal plant. These extracted substances may be used as precursors for the synthesis of various drugs. This definition helps us to distinguish between medicinal and non-medicinal plants. It clearly tells us plants which have been studied scientifically could be distinguished from plants which have not yet been studied scientifically, however both these classes might be considered as medicinal plants. For further assistance we can say almost all the plants possess various chemicals which might be applicable against some diseases. In ancient times, chemicals were not extracted, however plants, their leaves, seeds, stems, or other parts were given to patients against different diseases. It was a common observation that *Trachyspermum copticum* (Ajwain) was given to the patients with constipation. *Curcuma longa* (Turmeric) was used against various diseases. Modern studies

have revealed that these plants and various other plants are rich in chemicals which might be used against various diseases because of their antioxidant and antiviral properties. (Aneesa, Anitha, Varghese, & sciences, 2019; Asif, Hashmi, & Legumes, 2020; Damalas, 2011; Krup, Prakash, & Harini, 2013; Valiollahi et al., 2014; Verma et al., 2018)

It is observed that both these plants and various other plants possess flavonoids, saponins, octocosyl ferulate, 2',3'-dehydrosalonnol, ursolic acid, carnosol and rosmarinic acid which make them antioxidant, antiviral agents or potent anticancer drugs. For centuries traditional medicines were employed. Among these medicines blind trials were made to check their efficacy. However, these plants must qualify to be considered as medicinal plants. (Amoah, Sandjo, Kratz, & Biavatti, 2016; Balfour Jr, 1999; Ghoshal & Jacob, 1997; Liu, 1995, 2005; M. Petersen & Simmonds, 2003; M. Petersen, 2013; Sofowora et al., 2013)

Pharmacists and pharmacologists use a term of “crude drugs of natural or biological origin” for these plants. A more applicable and diverse definition of a medicinal plant should include following points:

- a) A plant as a whole or specific parts of plants should be utilized on galenical preparations i.e., medicinally e.g., Cascara bark
- b) Pure substances with medicinal applications could be directly extracted from plants or hemi synthesis of compounds possessing medicinal application is done by extracting them from plants. E.g., hemi-synthesis of sex hormones from *Dioscorea* yams)
- c) Plants which are used for food, spices and perfumery purposes may also possess the medicinal applications against various diseases, e.g., ginger, onion
- d) Isolation of antibiotics is carried out using microscopic plants, e.g., Actinomycetes are especially used for antibiotics isolation. Examples: *Streptomyces griseus*
- e) Surgical dressings are prepared by fibre plants, e.g., flax, jute and cotton are used for this purpose. (Elujoba, Odeleye, Ogunyemi, & Medicines, 2005; Kunle & Egharevba, 2009; Kurnik et al., 2008; Mothibe, Sibanda, & Medicine, 2019; Okigbo, Mmeka, & Technology, 2006; Sofowora et al., 2013)

Disease Prevention by the utilization of Medicinal Plants:

Strategies for the prevention of Communicable diseases:

There are three main approaches which help us to prevent from the communicable diseases. These include:

- Surveillance

- Outbreak investigations
- Immunisation

Unfortunately, most of the medicinal plants fail to play their role against these approaches. Most of the plants which have been used to extract traditional medicines enhance the immunity against several diseases. (Heczey et al., 2020; Heczey et al., 2014; Kouhi, Prabhakaran, Ramakrishna, & Technology, 2020; Straathof et al., 2020; Xu et al., 2019)

Strategies for Prevention of Non-Communicable Diseases

For the prevention of non-communicable diseases an action plan was given by World’s health organization which comprises of following points:

- Level of exposure of individuals and population to commonly modifiable risk factors, i.e., tobacco use, unhealthy diet and physical inactivity etc, should be reduced.
- A high-quality health care facility should be provided to people with noncommunicable diseases. (Balbus et al., 2013; Boutayeb, 2005; Islam et al., 2014; Puska, 2002; Rayner, Wickramasinghe, Williams, Mendis, & McColl, 2017)

Leading Causes of Deaths Globally

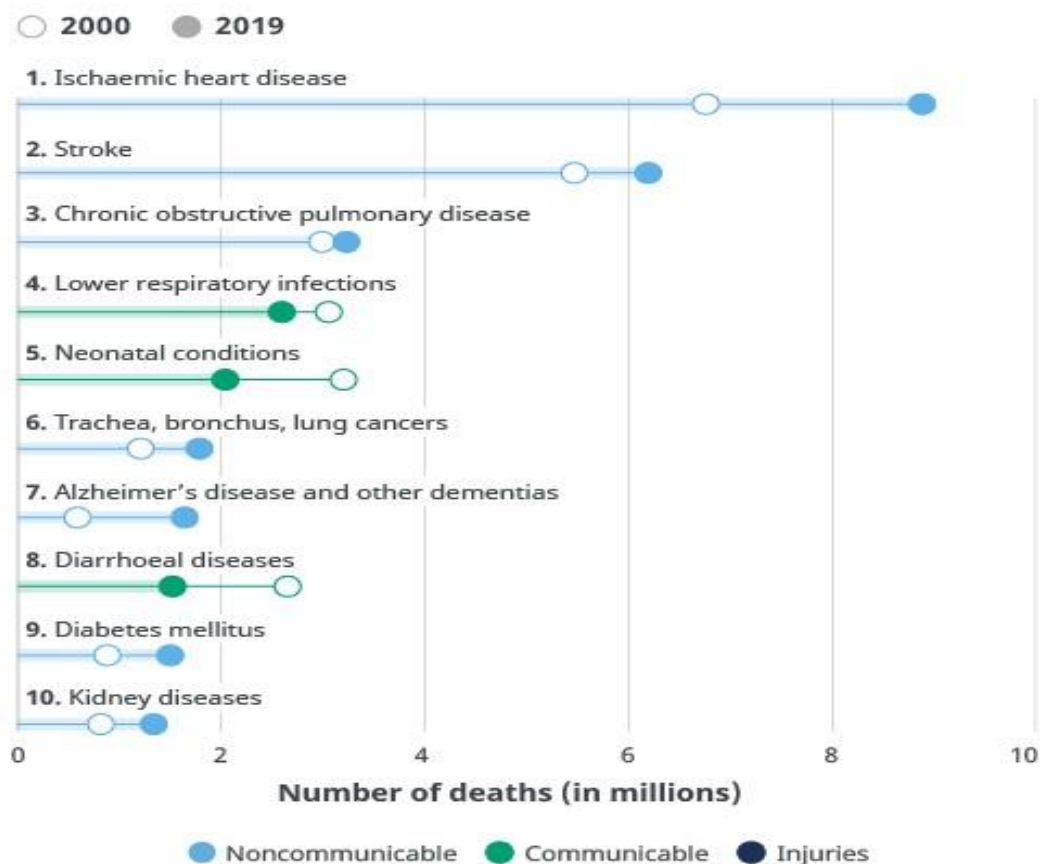


Figure 01: Leading causes of deaths globally, WHO global health estimates 2019

Source: WHO Global Health Estimates (Hoyert, 2022)

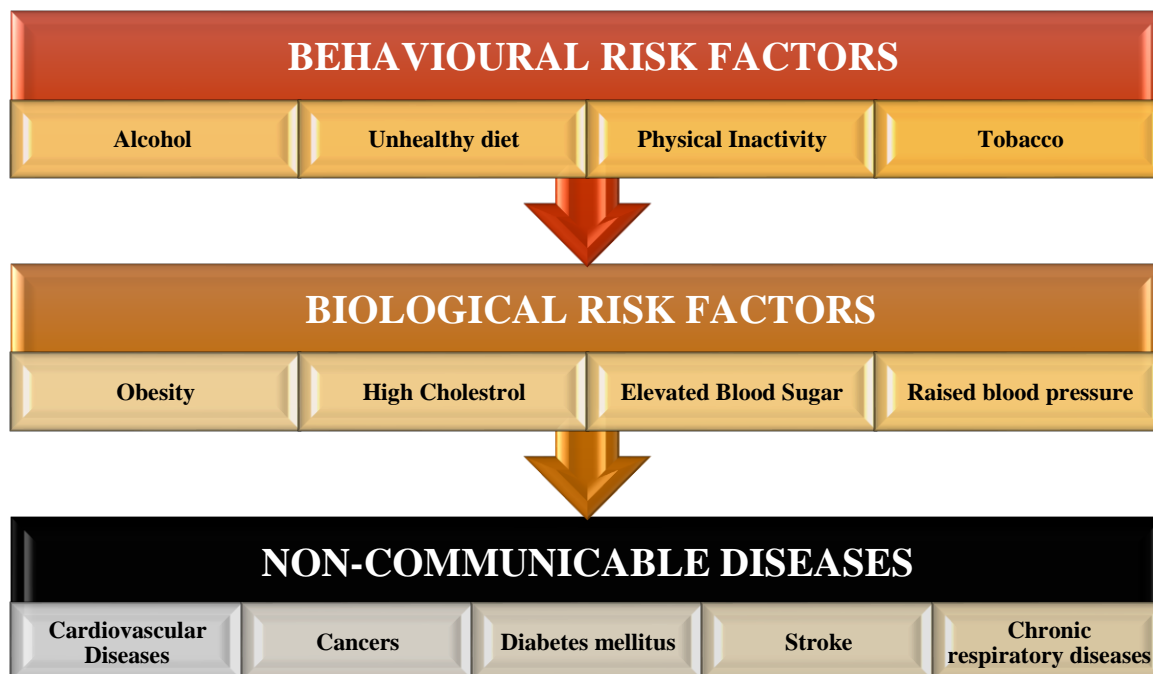


Figure 2: Chain of risk factors for Non-Communicable Diseases

In the light of above data, which has been retrieved from WHO’s recent publication, it is concluded that the death rate has been increased from 2000 to 2019 in case of noncommunicable diseases. So, measures should be performed to prevent noncommunicable diseases (NCDs).

MEDICINAL PLANTS TO PREVENT CANCER

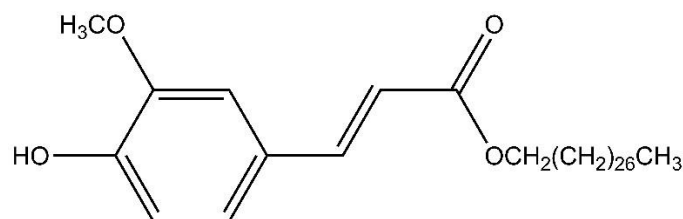
Yasukawa et al., 2012 has explained the methods, natural sources, crude drugs, foods, supplements and traditional herbal prescriptions possessing the chemo-preventive activity. He has stated in his review, cancer prevention is currently on the most urgent projects in public health. He describes about different stages of cancer. An experiment was performed, and it was observed the spread of cancer is carried out in three steps which results in the death of individuals. Firstly, cancer cells are initiated due to different behaviors like smoking and taking in the alcohols. Then after initiation, promotion and progression happens. Promotion might be considered as a reversible step and it takes too long to occur, however after progression the individual leads to death. So, if we try to prevent cancer in its initial stages, survival of the organism is possible. Environmental factors including diet is one of the most important

requirements for the prevention of these steps. (Aiello et al., 2019; Hosseini & Ghorbani, 2015; Onouchi et al., 2012)

1) *Prunus* spp. (Family Rosaceae) e.g. African Prune:

A good example of chemo-prevention is prostate cancer as its growth rate is very slow as compared to other cancers and it is mostly diagnosed in elderly males. In Europe, the treatment of prostate cancer is carried out by the extract of *Pygeum africanum* (*Prunus Africana*) as it contains ethanolic extracts upto (30%) of the bark which has an ability to inhibit PC3 and LNCaP cell's growth. It helps in the induction of apoptosis which may alter the cell kinetics which may slower down the spread of prostate cancer. Moreover, it has been studied that *P. africanum* has a significant role in regulation of prostate cancer both in *in vivo* and *in vitro*, so it might considered a useful supplement against the people with prostate cancer at high risks. Isoflavones and other chemicals which might be found in legumes may be proven helpful in this regard. (Baraket, Abdallah, Ben Mustapha, Ben Tamarzizt, & Salhi-Hannachi, 2019; Donia, Ghada, Hend, Sana, & Amel, 2016; Sonika, Jaya, Pankaj Kumar, Swaha, & Arjun, 2016)

Octacosyl ferulate has inhibited tumor promotion in mouse skin by DMBA/TPA. It is extracted from some of the plants present in Rosaceae family. Chemical structure of Octacosyl ferulate is as following:



(*E*)-octacosyl 3-(4-hydroxy-3-methoxyphenyl)acrylate

Figure 04: Octacosyl ferulate (A compound extractef from Pruni Cortex)

2) *Azadirachta indica* (Family Meliaceae) Neem

Studies has revealed that more than 60 types of biochemicals could be extracted from Neem plant which may include steroids and terpenoids. It has been studied that this plant contains compounds which possess the ability to prevent, protect and suppress tumors. Triplenegative breast cancer (TNBC) which account for approximately 15-20 percent of all breast cancers is unfortunately difficult to treat. Treatment options for this type of cancer are very limited. However, it has been studied that a compound 2'-3'-dehydrosalannol (DHS) has been extracted

from *Azadirachta indica* uncrushed leaves has an ability to inhibit apoptosis in TNBC cell lines. Also, neem leaves inhibited the cancer in mouse skin, which confirms the ability of this compound to act as a preventive measure against cancers. (Akhila & Rani, 1999; Alzohairy, 2016; Biu, Yusufu, & Rabo, 2009; Prashanth, Krishnaiah, Technology, & Science, 2014; Rahmani, Almatroudi, Alrumaihi, & Khan, 2018; Shareef & Akhtar, 2018; Sujarwo, Keim, Caneva, Toniolo, & Nicoletti, 2016)

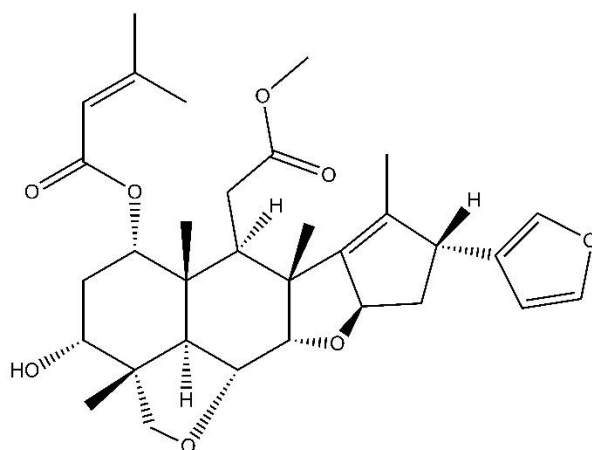
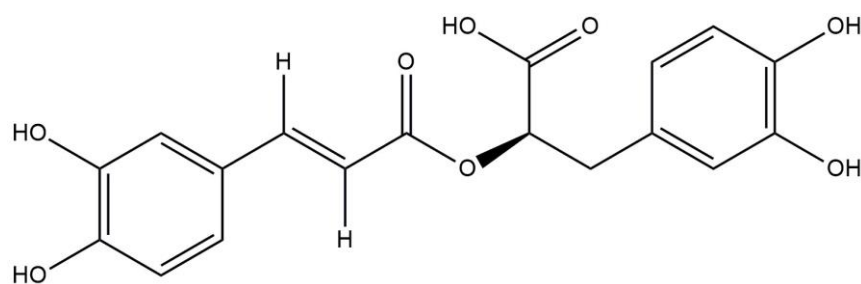


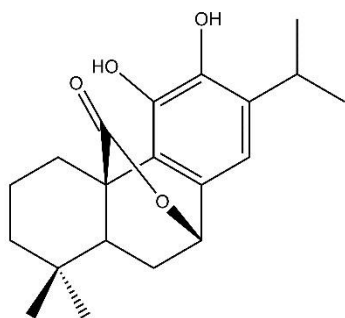
Figure:05 2'-3'-dehydrosalannol (DHS) a potent inhibitor against TNBC

3) *Rosmarinus officinalis* L (Family Labiatae) Rosemary

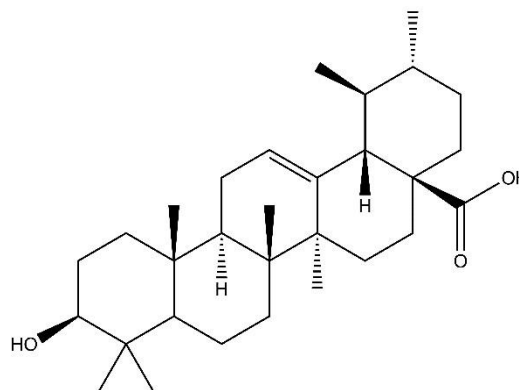
Studies have revealed that, colorectal cancer is one of the major cancers which resulted in deaths in Australia. Protective effect of rosemary on colorectal cancer and other types of cancer has been examined. Carnosol, carsonic acid, ursolic acid and rosmarinic acids have been found in the plants of this family which possess anticancer activity. Studies have been made and it showed strong inhibition effect predicted by all these compounds. López-Jiménez (2013) demonstrated that rosemary extracts possess carnosol and carsonic acid which may exhibit antiangiogenic activity resulting in contribution as a chemo preventive and acting as inhibitors in angiogenesis related malignancies. Chemicals extracted from rosemary plant has been illustrated in following figure. (González-Minero, Bravo-Díaz, & Ayala-Gómez, 2020; Inatani, Nakatani, Fuwa, & chemistry, 1983; Nakatani, Inatani, & Chemistry, 1983; Nieto, Ros, & Castillo, 2018; M. Petersen & Simmonds, 2003; Stefanovits-Bányai, 2003)



Rosmarinic Acid



Carnosol

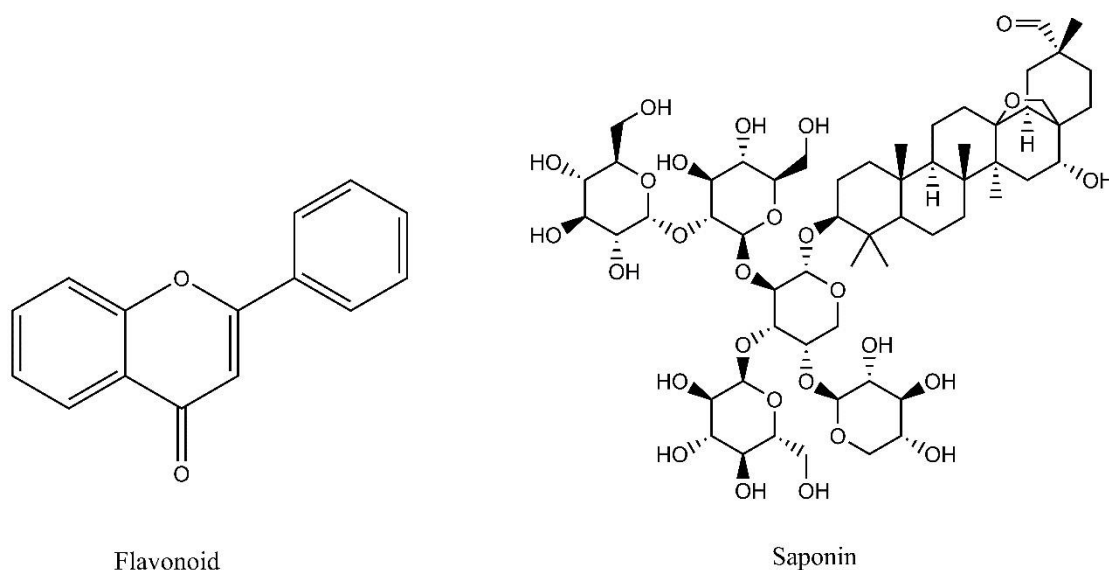


Ursolic acid

Figure 06: Chemical structures of Rosmarinic acid, Carnosol and ursolic acid.

***Glycine max* or *G. soya* (Family Leguminosae) Soya milk**

Genistein is one of the most abundant phytoestrogens which is found in soya beans. It has an ability to bind to oestrogen receptors. This binding may result in performing the anticancer activity. Compounds which may be found in soya milk include iso-flavonoids and saponins which have been shown to exhibit phytoestrogenic activity. Studies have revealed that soy isoflavones consumption may result in protection against breast cancer development, however premenopausal women are advised not to take soy in-flavones as adverse effects have also been studied in this class. Structure of chemicals extracted from this class are shown as following. (Adzu & Haruna, 2007; Borgi, Recio, Ríos, & Chouchane, 2008; BRAR & CARTER JR, 1993; Massey, Palmer, Horner, & chemistry, 2001; Nwokolo, 1996; Pan, Su, Cai, & Wu, 2017; Rodrigues et al., 2005; Shamsudin et al., 2022; Waqas et al., 2015; Welty, Ali, Nguyen, & Jhamnani, 2011)



Flavonoid

Saponin

Figure 07: Chemical structures of Flavonoid and Saponin

CONCLUSION

In this review, some of the valuable medicinal plant families and chemicals extracted from them have been identified and presented which may be used as potent anticancer drugs. All these compounds and many others which are accumulated in high quality in these plant families could be extracted and studied against various types of cancers. Their inhibitory effect, structure compatibility, hydrophobic ends, and ability to bind with proteins restrict the division of tumor cells. Almost all the parts of these plants possess different types of chemicals and different inhibitory effects. It is a brief review which included only a few plants. However, many other plants belonging to these families could be studied to prevent different types of cancers.

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