

Role of Herbals as Anti-Cancer and Anti-Inflammatory Agents

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Abstract:- Cancer is now recognized as one of the most common diseases in the world, due to its high mortality rate. Inflammation is our body's immune system against potentially dangerous stimuli like allergens and/or tissue damage. However, a variety of disorders, including allergies, cardiovascular issues, metabolic syndrome, cancer, and autoimmune diseases are the underlying cause of uncontrollable inflammatory response. Inflammation is directly linked to cancer and plays an important role in the growth and development of tumour. Inflammation and cancer are linked through the extrinsic and intrinsic processes, respectively. Herbals play a very important role in treatment of cancer and inflammation. Several plant derived extracts inhibit and regulate signaling process and network associated with the growth as well as proliferation of cancer cells. It is necessary to invent new strategies to prevent and treat disease. Products obtained from plants are a valuable source for the development of novel medications, due to their diverse chemical composition. So researchers are focusing on various phytoconstituents and how well they may work against various diseases at the moment. The present review is therefore an effort to give the literature study for Mechanism, relation between inflammation and cancer and the list of medicinal plants that possessed anti-inflammatory and anticancer activity.

Keywords:- Anti-Cancer; Anti-Inflammation; Herbals; Relation between Inflammation and Cancer.

I. INTRODUCTION

Herbal medicines have special significance in the public, cultural and traditional medicine systems of India. The origin of the present health care system is plant based medicine and is accepted for their economic importance also. Herbal medicines are employed as lead molecules in the development of new drugs as well as directly as

therapeutic agents. Present study and understanding recommend that the use of herbals can give true benefits on health when used long-term.

➤ Cancer

Cancer is one of the leading causes of death worldwide, with uncontrolled multiplication of unwanted cells causing tissue damage. According to a survey by the global Agency for Cancer Cases research, 7.7 million men and 6.9 million women were diagnosed with cancer worldwide in 2012, with the number expected to rise to 24 million by 2035. Lung, breast and colorectal cancers are the most frequent cancers. It is responsible for one-fourth of all cancers in women. In general, cancer is on the rise in emerging countries as a result of lifestyle changes such as dietary changes. Herbal remedies are exclusively utilized in the treatment of different types of diseases because of less toxicity in comparison to modern allopathic medicines [1].

Various chemo protective agents are used in the treatment of cancer, but their adverse effects on the body make their use undesirable [2]. Solid tumors are typically a component of normal tissues and in the right circumstances can either spread through the connective system to colonies distant areas in the body or attack nearby tissues. Nearly 90% of cancer-related deaths are due to these secondary tumors, or metastases. The sixth and last characteristic of cancer is the ability of tumor cells to target and grow. Tumors can thrive and spread by metastatic processes in new habitats with no space or nutritional constraints [3].

One of the main causes of cancer is a gene mutation. These mutations can happen after birth or can be inherited, and they can be brought on by a variety of factors, including alcohol, smoking, an imbalanced diet, pollution (pollutants), hormones, chronic inflammation, and infections that contribute to cancer. *Fig. 1* describes various causes of cancer.

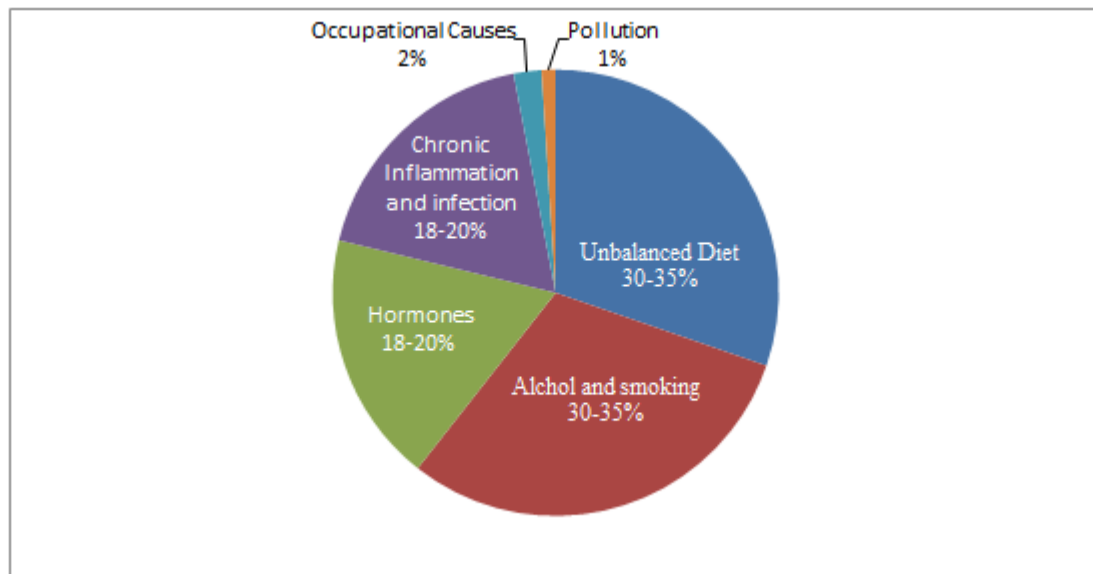


Fig 1 Different Causes of Cancer

- *Types of Cancer:*

Cancer is divided into six parts. It includes **skin cancers** (Basal cell carcinoma, Melanoma, Squamous cell carcinoma), **Cancers in women** (Breast, Ovarian, Gynecological and Choriocarcinoma) **cancers of digestive systems** (Esophageal, Stomach, pancreatic, Liver, Colon, Rectal, Anal cancer) **cancers of urinary system**(Kidney, Bladder, Testis and Prostate cancer) **cancers of blood and lymphatic system**(Hodgkin's disease, Leukemia's, Lymphomas, Multiple myeloma, Waldenstrom's disease and **Miscellaneous cancers** (Brain, Bone, Choriocarcinoid, Nasopharyngeal, Retroperitoneal sarcomas, Soft tissue and Thyroid cancer)[4].

- *Cancer Development:*

The formation of cancer is considered to be a multiple step procedure at the cellular level that includes mutation and the selection of cells with high proliferation, survival, invasive, and metastatic potential (*Fig. 2*). The first stage of the development is **Tumor initiation**, supposed to be the result of alteration in gene to facilitate an uncontrolled single cell proliferation. A population of clonally generated tumour cells expands after cell proliferation. As the tumour grows, new mutations keep occurring in the cells that make

up the **tumour progression**. Some of these mutations provide a selective advantage on the cell, such as rapid growth, and as a result, the progeny of a cell with that mutation will overtake all other cells in the tumour population. The process is known as clonal selection since a new clone of tumour cells has evolved due to its quicker growth rate or other features (including survival, invasion, and metastasis) so as to give a selective advantage. Throughout tumor development, clonal selection occurs, causing tumors to continuously grow more quickly and become more dangerous.

II. INFLAMMATION

Inflammation is our body's immune system against potentially dangerous stimuli like allergens and/or tissue damage. However, an uncontrollable inflammatory reaction is the underlying reason of a variety of disease, including allergy, heart related problems, cancer and autoimmune diseases all of which have a significant financial impact on both individuals and society. Cyclooxygenases (COXs)

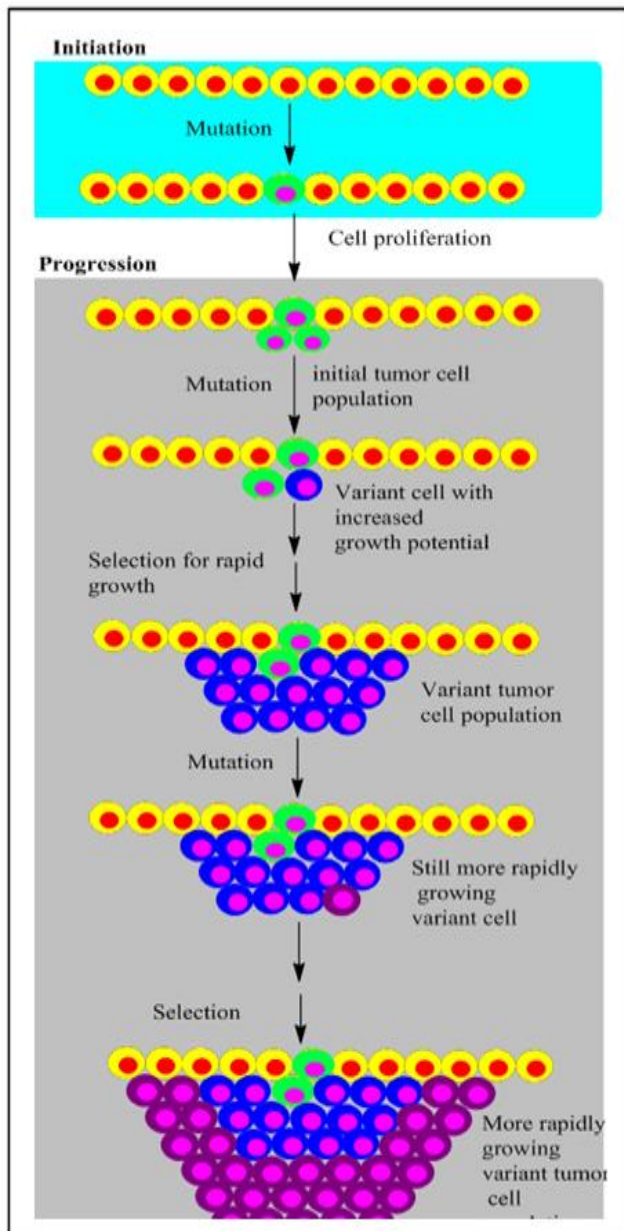


Fig.2 Development of Cancer

such as cyclooxygenase-1 (COX-1) cyclooxygenase-2 are key enzymes in the formation of prostaglandins, prostacyclins and thromboxanes which are related to inflammation, pain and platelet aggregation (COX-2) [6].

➤ Types of Inflammation

Inflammation can be classified into two types: acute inflammation and chronic inflammation depending on how long an illness has been present. Acute inflammation lasts for a few days or weeks and is the body's initial reaction to harmful stimuli. Granulocytes account for the majority of the invasive inflammatory cells in acute inflammation. The simultaneous occurrence of tissue apoptosis and regeneration defines chronic inflammation. Macrophages and lymphocytes are the major immune cells that invade sites of chronic inflammation. Chronic inflammation, autoimmunity, tissue fibrosis, and necrosis will arise from inability to eradicate the pro-inflammatory stimuli during the acute inflammation phase [7]. Sepsis like inflammation,

Coagulopathy, respiratory and cardiovascular complications is more serious complication of COVID-19. The innate immune system develops early inflammatory responses in response to injury or infection to prevent further illness and to facilitate the adaptive immunity in producing long time, host-protective Antibody and T cell responses against the viral within 7–10 days after infection. On the other hand, as inflammation is not controlled or resolved subsequent to satisfy its original purpose, it develops into chronic hyper-inflammation, which inhibits adaptive immune Responses and causes tissue injury [8].

➤ Inflammation in Cancer

It is crucial to know the mechanism of inflammation in cancer. Infection, chronic inflammation, or autoimmune disease occurs at the same tissue or organ location in about 20% of all cancer cases. Examples chronic hepatitis, inflammatory bowel disease and gastritis brought on by helicobacter which successively increase the risk of Liver cancer, colorectal cancer and stomach cancer. The most commonly mutated tumor suppressor gene is Tp53, which codes for the P53 protein and has multiple roles in regulating cellular homeostasis. One of these roles is its transcriptional antagonistic relationship with nuclear factor KB an important factor in the positive regulation of inflammation. The decrease p53 proteins lead to an increase in the expression of NF-KB activates signals that are always present in the tumor microenvironment and even in the normal tissue [9].

III. MECHANISM

It is particularly obvious that cytokines and chemokines released throughout inflammation can cause cell alteration. The cellular level mechanisms are still difficult. JAK-STAT pathway, TGF B pathway, TNF-alpha, NF-KB, Arachidonic acid metabolism pathway, COX and LOX pathway are six important cellular pathways that involved in tumor progression. Here we detailed the NF-KB Pathway.

The immune system and inflammation both are regulated by transcription factor NF-KB. Some cancer cells depend on the NF-kB pathway for survival because it inhibits tumour suppressors like p53 and promotes cell proliferation and preventing cell death.

Numerous pro-inflammatory ligands and their receptors, such as cytokines, pattern-recognition receptors (PRRs), TNF receptors, and T-cell receptors, activate the NF-kB pathway. The existence of two distinct mechanisms for NF-kB signalling has been established. TNF- α , IL-1, or TLR stimulate the "canonical" pathway, which in turn stimulate the IKK's activation of IKB α phosphorylation (Fig. 3). p50/Rel-A or p50/c-Rel dimers associate with and inactivate the IKB α protein. IKB α is encouraged to be degraded by the ubiquitin-proteasome pathway through phosphorylation. As a result, Rel-A/p50 i being released, it moves into the nucleus, wherever it stimulates the expression of chemokines, cell cycle regulators, anti-apoptotic proteins, and pro-inflammatory cytokines. This signalling cascade's downstream effect includes the

development of cancer, necrosis, or tissue inflammation. LTs, CD40L, or BAFF activate the non-canonical NF- κ B pathway, which in turn activates IKK and triggers the release of the p100/Rel-B dimer into the nucleus (Fig 3). Tumor genesis, tissue necrosis, and inflammation are all caused by both pathways.

IV. LINK BETWEEN INFLAMMATION AND CANCER

Inflammation and cancer are linked via the extrinsic and intrinsic processes, respectively (Figure 4). The

extrinsic pathway is initiated by inflammatory factors to enhance the chance of developing cancer, while the intrinsic is carried on through genetic changes which causes inflammation and cancer. The release of inflammatory cytokines, which activate certain transcription factors like NF- κ B, connects both pathways. When NF- κ B is activated, growth factors, metalloproteases, and other inflammatory mediators are secreted, which helps to create an inflammatory tumor microenvironment [10]. The development and spread of cancer is significantly influenced by a number of cellular elements of the inflammatory process [11,12].

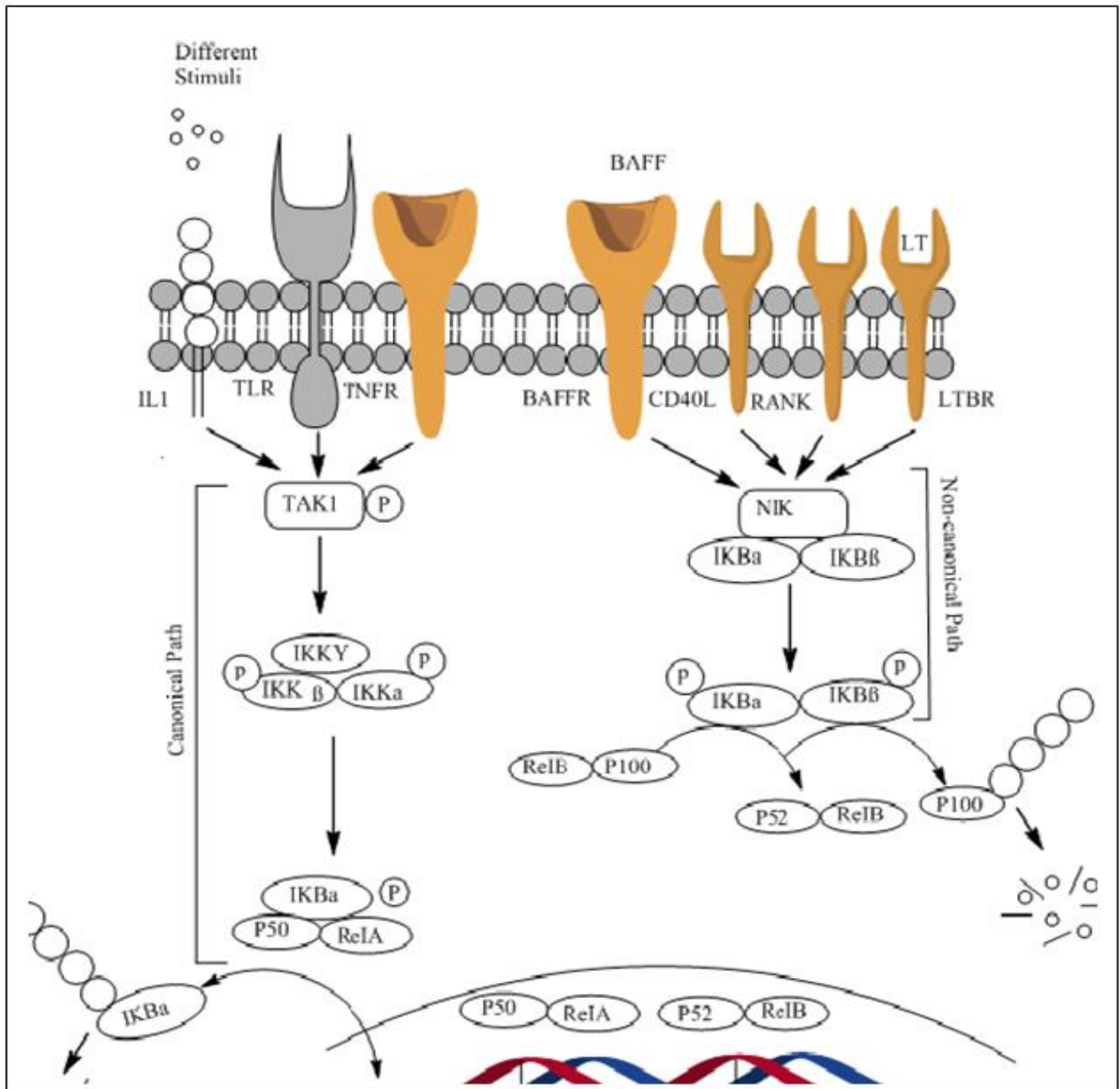


Fig 3 Mechanism of Tumor Progression by Inflammatory Pathway

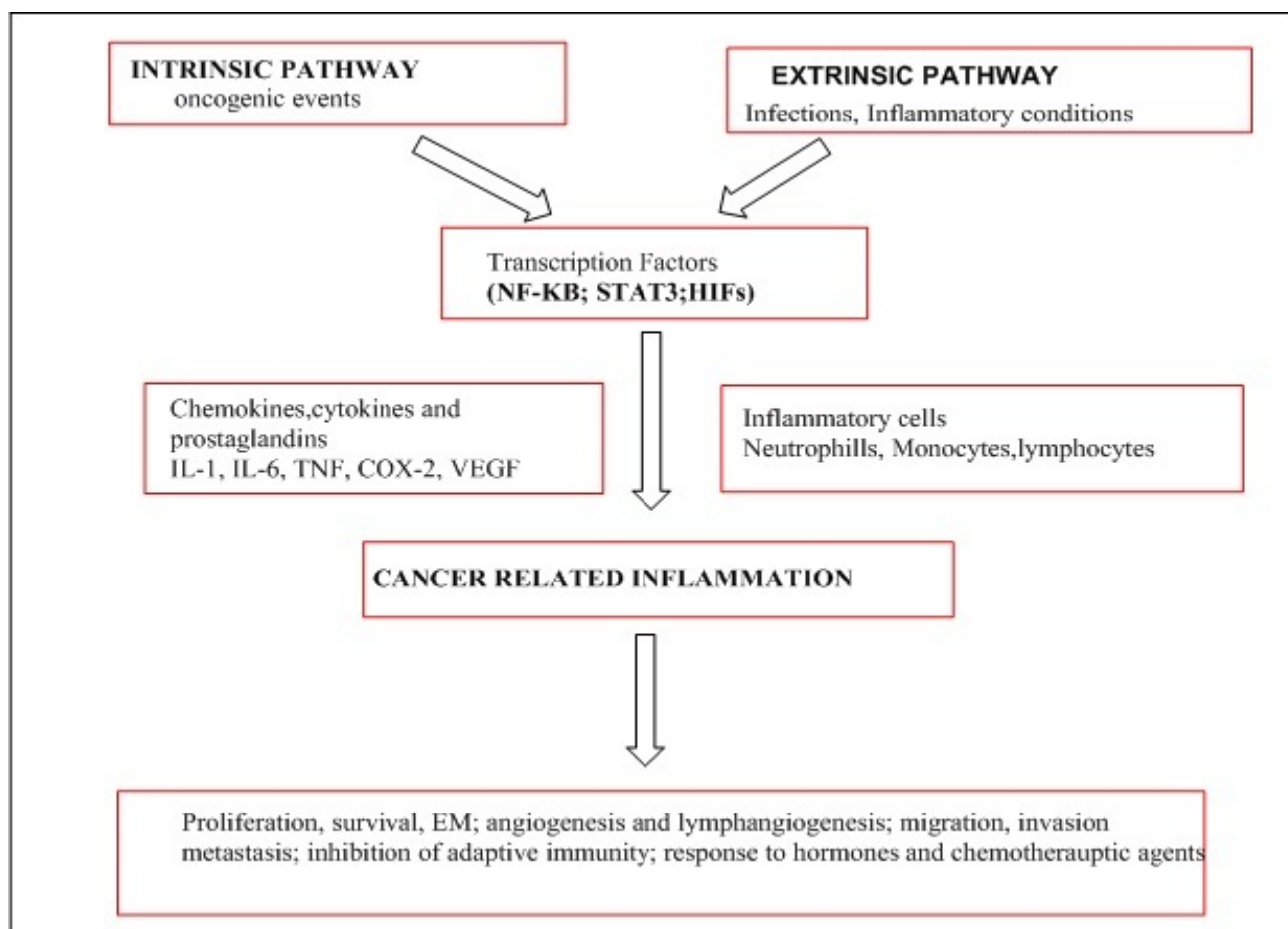


Fig 4 Pathways Relating Inflammation and Cancer

V. HERBS WITH ANTICANCER ACTIVITY

Herbal remedies play a beneficial role in cancer treatment. These have been utilized for the treatment of large range of medical disease in India since centuries. It uses plants or a combination of plant extracts to treat disease and advance wellness. One of the most popular complementary and alternative cancer treatment options is herbal therapy [13].Some of the vital medicinal plants are Amla, Zinger, Tulsi, Vinca, Tea, Indian abutilon, Wiry indigo, Datura, Asoka, Crocus sativus, Gotu kola, Brahmi, Bidi leaf tree, Sponge guard, Mango, Brahmi, Saffron and Indigofera aspathaloides that demonstrated the anticancer activity.

Table 1 List of Some Medicinal Plants with Anti-Cancer Potential

Sr . No	Name	Biological source	Extraction Method	Part used	Chemical constituent	Reported action	Referen ces
1.	India abutiln	<i>Abutilon indicum</i> (Malvaceae)	homogenizat ion	Leaves	β-sitasterol, Vanillic, p-coumaric, acceic, fumaric and amino acids,alantaolactone, isoalantolactone etc.	Lung cancer	[14,15]
2.	Wiry Indigo	<i>Indigofera aspalathoides</i> (Fabac eae)	Maceration	Leaf	Alkaloids, saponin, tannins, steroids, flavonoids and anthraquinone	Antitumor	[16,17]
3.	Asoka	<i>Saraca asoca</i> (Caesalpinaceae)		Flower	Gallic acid ⁷ , leucocyanidin Oleic, linoleic, palmitic, stearic acids, β-sitosterol,quercetin,apigenin, glucoside,Pelargonidin ³ ,5digl ucoside and cyanidin-3	Lukemia cancer, lung cancer	[18,19]
4.	Jimson	<i>Datura</i>		Seed and	Hyoscyamine and scopolamine	Breast cancer	[20]

	weed	<i>Stramonium</i> (Solana ceae)		root		cells	
5.	Gotu kola	<i>Centella asiatica</i> (Umbelliferae)	homogenization	Fresh and dried leaves and stem	Triterpene acid, Asiatic acid and terminolic acid	anti-neoplastic, Human respiratory epithelial cell	[21,22]
6.	Brhami	<i>Bacopa monera</i> (Family)	Maceration	Whole plant	Bacopasides I and II, stigmasterol, β -sitosterol, aglycones, betulinic acid, proteins like α -alanine, aspartic acid, glutamic acid, and serine along with sugars D-mannitol,	Breast cancer, colon cancer, liver cancer, glioblastoma and neuroblastoma	[23,24]
7.	The Bidi leaf tree	<i>Bauhinia racemosa</i> (Caesalpiniaceae)		Bark, leaves	β -amyrin, β -sitosterol, kaempferol, quercetin, scopoletin, scopolin and tannins.	Antitumor	[25,26]
8.	Saffron Crocus	<i>Crocus sativus</i> (Iridaceae) <i>stokes</i>		Flower	crocin, crocetin, and safranal	Gastro-intestinal cancer, lungs cancer, prostate, colon cancer	[27,28]
9.	Vegetable Sponge gourd	<i>Luffa cylindrical</i> (Cucurbitaceae)	Maceration	Leaf	volatile organic compounds ranging from alcohols, triterpenes, phenols, fatty acids, esters, and steroids	Colon cancer	[29]
10.	Mango	<i>Mangifera indica</i> (Anacardiaceae)		Leaf	Mangiferin, isomangiferin, mangiferin-6-O-gallate, mangiferin 3-methyl ether	Breast cancer cells	[30,31]
11.	Tea	<i>Camellia sinensis</i> (Theaceae)	solid phase extraction	flowers	Tea catechins, amino acids, caffeine, carbohydrates, proteins and vitamins	Anti-tumor	[32]
12.	Amla	<i>Emblica officinalis</i> (Euphorbiaceae)	Decoction	Fruit	Gallic Acid, Quercetin, Quercetin-3- β -Dglucoside, Quercetin-3-O-rutinoside, β -Sitosterol, Phytate, Tannin and saponin	Breast cancer, human colorectal and neuroblastoma cancer	[33,34]
13.	Red ginger	<i>Zingiber officinalis</i> (Zingiberaceae)	Maceration	Rhizomes	Camphene, geranial, geranyl acetate, vanilloids, sesquiterpenes,	anticancer activity against A549, SKOV-3, SK-MEL-2, and HCT15 cancer cells	[35,36]
14.	Tulsi	<i>Oscimum Sanctum</i> (Lamiaceae)	Maceration	leaves, seeds, and roots	Camphor, other aromatic monoterpenoids such as limonene and Ocimene	inhibited tumor cell proliferation, Lukemia cancer	[37,38]
15.	Vinca	<i>Catharanthus roseus</i> (Apocynaceae)	Maceration	Whole plant	Vincristine, vinblastine, catharanthamine	Cancer treatment	[39]

VI. HERBALS WITH ANTI-INFLAMMATORY ACTIVITY

Tree, Priyangu, Job's tear, Garlic, Bhang, Jimson weed, Licorice, Guggule, Pudina.

Medicinally important plants with anti-inflammatory potential involves India abutilon, Papaya

Stinging nettle, White lily, Witch hazel, Neem, Cognograss, Wiry indigo, Setawar, Afarican monography, Mango,

Table 2 List of Some Medicinal Plants with Anti-Inflammatory Activity

S r. No	Name	Biological Name	Type of extract/extraction method	Part used	Chemical constituent	Reported action	References
1.	Witch hazel	<i>Hamamelis virginiana</i> (hamamelidaceae)	purchase extract	Fresh and dried leaves	Tannins, manalolyl hamamelosin	Astringent, antiinflammatory, hemostatic effect	[40,41]
2.	Setawar, miracle leaf	<i>Kalanchoe pinnata</i> (crassulaceae)		Leaf stem and root	Bufadenolide, cardiac glycoside	Antiinflammatory, applied to wounds and burns	[42]
3.	Magnolia	<i>Magnolia flos</i> (magnoliaceae)	Maceration	Whole plant	Magosalin, magnosalicin, magnone A, B, magnolin, eudesmin), α -pinene, cineole, citral, eugenol, and capric acid	Anti-inflammatory	[43]
4.	Neem	<i>Azadirachta indica</i> (meliaceae)	Cold maceration	Bark, leaves and seeds	Nimbin, nimbanene, 6-decacylnimbenin, nimbandiol, nimbolide	Antimicrobial, antifungal, inflammation of gums, gingivitis	[44,45]
5.	Priyangu	<i>Callicarpa macrophylla</i> (Verbenaceae)		Root, Bark, Leaves, Flowers, Fruits	Phyllocladane diterpenoids calliterpenone and calliterpenone monoacetate	anti-inflammatory	[46,47]
6.	Stinging nettle	<i>Urtica dioica</i> (urticaceae) <i>Nettele</i>	Maceration	Fresh and dried flowering plant and root	B-sitosterol, lectins, polysaccharide	Antiinflammatory and diuretic	[48,49]
7.	Bhang	<i>Canabis sativa</i> (cannabaceae)	Maceration	Seeds	Lignanamide, coumaroylaminoglycoside	Neuroanti-inflammatory	[50]
8.	African monograp hy	<i>Khaya senegalensis</i> (meliaceae)	Maceration	Leaf and stem bark	khayasin, ivorenolide, limonene	Antiinflammatory and cardiogenic	[51,52]
9.	Garlic	<i>Allium sativum</i> (Amaryllidaceae)		Bulbs	Ajoenes, allicin, vinyl dithiols, Diallyl sulfide, Diallyl disulfide, Diallyl trisulfide, Allyl methyl sulfide	Neuroinflammation	[53,54]
10.	White lily	<i>Lilium candidum</i> (liliaceae)	UAE	Fresh and dried bulb	Isorhamnetin glycosides, steroid, steroidal glycoside	Treatment of skin inflammation	[55,56]
11.	Cogongrass	<i>Imperata cylindrical</i> (gramineae)		Leaves and stem	lignans, graminone A and B	Diuretic, antiinflammatory	[57,58]
12.	Mango	<i>Mangifera indica</i> (anacardiaceae)	Maceration	Mango leaves	Mangiferin, proanthocyanic acid, catechin and isoquercetin	Astringent, antiscorbic and antiinflammatory	[59,60]
13.	The Bidi leaf tree	<i>Bauhinia racemosa</i> (Caesalpinaceae)		Bark, Leaves	B-amyrin, β -sitosterol, kaempferol, quercetin,	Anti-inflammatory	[61,62]

					scopoletin, scopolin and tannins.		
1 4	Job's tears	<i>Coix lacryma-jobi</i> (Gramineae)	Maceration	Stem and leaves	Starch, crude proteins and lipids.	Inflammatory diseases and rheumatism.	[63,64]
1 5	Liquorice	<i>Glycyrrhiza glabra</i> (leguminose)	Decoction	Roots and stems	Glycerizin, glycyrrhithinic acid	Anti-inflammatory, for treatment of allergic rhinitis	[65,66]
1 6	Guggule	<i>Commiphora wightii</i> (Burseraceae)		Stem	Z-guggulsterone, E-guggulsterone, Z-guggulsterol and guggulsterol I-V.	Inflammatory and antiarthritic activities	[67,68]
1 7	Ashwagandha	<i>Withania somnifera</i> (solanaceae)	Maceration	Root	Protein, amino-acids, carbohydrate, steroids, alkaloids, oxalic acid, flavonoids, phenolic compounds, tannis, withanoloides, inorganic compounds and saponins	Anti-inflammatory	[69,70]
1 8	Papaya	<i>Carica papaya</i> (caricaceae)	Soxhlet	Leaves and fruits	Carpine, pseudocarpine, glucosinolate, saponins	Analgesic and antiinflammatory	[71,72]
1 9	Pudina	<i>Mentha piperita</i> L. (Lameace)		leaves and flowering tops	Limonene, methone, cineole, menthofuran,	Anti-inflammatory, Allergy	[73,74]

VII. CONCLUSION

This study gives an overview of relation between inflammation and cancer, how they co-relates and mechanism and pathway involved in this process. In this review list of medicinal plants possessed anti-inflammatory and anti-cancer activity have been presented. We can conclude that this literature study will really help the researcher for further study.

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