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A REVIEW ON CRUDE DRUGS AS ANTICANCER AGENTS

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ABSTRACT

Cancer is still the world's biggest cause of death, despite enormous advancements in both the creation of innovative cancer treatments and basic cancer biology. Cancer's etiopathogenesis is intricate. In addition to genetic susceptibility, diet, lifestyle, and exposure to environmental pollutants are recognized environmental variables linked to cancer. High rates of cancer death are a result of treatment toxicity and eventual cancer return. The cancer treatments that are currently available, such as thermotherapy, radiation, chemotherapy, and surgery, are not at all curative for numerous cancer types. Despite being the most often used cancer treatment, chemotherapy in particular is typically linked to a range of severe adverse effects. This succinct review aims to compile recent research on a few basic medicines with a particular emphasis on their therapeutic targets and helpful roles in cancer treatment and chemoprevention. It is thought that crude medications have neutraceutical effects on cancer patients, even if their pharmacological processes and biochemical roles in cancer biology and tumor chemoprevention are not entirely understood.

KEYWORDS: Crude drug, cancer, inflammation, cell cycle, apoptosis.

INTRODUCTION OF CRUDE DRUGS

Many potent medications have been developed over the course of medical history from organic plant or animal extracts. For instance, quinine, an anti-malarial medication, is taken from the bark of the Cinchona tree. This fact may indicate to us that nature contains a greater quantity of primary anticancer medications. People have been employing plant rhizomes,

leaves, barks, and other natural materials soaked in alcohol or wine as medicines to treat illnesses since ancient times in the East, particularly in China and Korea. Crude medications are those that originate from plants. The mounting data showing diets high in fruits and vegetables can lower the incidence of certain chronic diseases signals the significance of natural medicine sources. such as diabetes, heart disease, cancer, etc.[1,2] The search for basic treatments has therefore grown more crucial as the incidence of cancer is rising and there are currently no effective medications for treating the disease that don't have serious side effects. Thankfully, advances in biochemical technology and molecular biology have encouraged the study of crude pharmaceuticals. The production of crude pharmaceuticals and their general availability have been made possible by new purification and analytical methods[3], which have also produced notable success in the study of cancer biology and tumor treatment.[3] Raw materials can be employed as standalone treatments, or their active components can be used directly or as supplementary treatments in clinical settings to treat cancer. Furthermore, pro-drugs experts employ crude pharmaceuticals as a starting point for screening for more effective anti-cancer medication precursors or in other ways that benefit them.

Examples of crude drugs as anticancer agents

Plant phytochemicals are thought to be responsible for the beneficial benefits of crude medicines components of plant-based diets), including fibers, phenolic chemicals, terpenoids, steroids, indoles, and carotenoids.[3] These are the efficient components thought to lower the risk of cancer. We include a number of phytochemicals that are either currently being utilized or may one day be used to treat cancer below.

Paclitaxel

The medicine Paclitaxel, also known as Taxol, is a widely used and effective cancer treatment that has been approved to treat many tumors. It is currently being evaluated for the treatment of coronary heart disease and Alzheimer's disease. Figure 1A illustrates this. It is a crude medicine success story as a result. Paclitaxel, which belongs to the natural organic chemical family known as terpenoid, was extracted from the bark of the slow-growing and endangered Taxus brevifolia, a member of the Taxacae tree family. It was initially taken from the Yew tree in the US in 1971, and by 1992, the US Food and Drug Administration (FDA) had approved it for use in clinical settings. These days, paclitaxel has shown promise in the treatment of numerous cancer types, including ovarian[1,2,4,5], breast[1,5,6], lung[7, 8], and esophageal[9], among others & malignancies of the liver.[10] Paclitaxel exhibits distinct

properties such as selective and reversible binding to β-tubulin within the microtubule, with a stoichiometry of nearly one (in comparison to the α,βtubulin dimer)[11,12], inhibition of cell division, blocking of cell mitosis, stabilization of cytoplasmic microtubules, and induction of the formation of the recognizable microtubule bundles in cells.[13]

Curcumin

Numerous naturally occurring substances derived from fruits and vegetables are being researched for their possible medical benefits in addition to paclitaxel, also known as Taxol. For instance, curcumin, which comes from the plant Curcuma longa and is depicted in Figure 1B, is used in Chinese medicine and as the yellow coloring agent in turmeric, an Indian traditional dish. It is recognized for its anti-inflammatory, antiviral, antibacterial, antifungal, and antioxidant properties and may also be able to treat a number of other conditions, such as diabetes, allergies, arthritis, and Alzheimer's disease.[14] In their paper on curcumin, Goel et al.[15] proposed that since deregulation of up to 500 distinct genes is the primary cause of most malignancies, substances, Multiple gene-targeting compounds, including curcumin, are essential for both cancer prevention and treatment. Curcumin has been demonstrated in research to far to interact with a broad range of proteins and alter their expression and activity. These proteins include transcription factors, inflammatory cytokines and enzymes, and gene products associated with angiogenesis, invasion, proliferation, and survival of cells.[15] There were 22 active Phase I or II clinical trials employing curcumin connected to cancer as of 2007.[16] Numerous of these studies suggest that curcumin is safe and might have therapeutic benefits. For instance, curcumin has stopped the growth of several tumor cells in culture, stopped malignancies in rats caused by carcinogens, and inhibited the development of human cancers in animal models used for xenotransplantation or orthotransplantation, either by itself or in conjunction with radiation or chemotherapy drugs.[14] According to recent research, curcumin reduced the lifespan of RT4V6 and KU7 bladder cancer cells, at least in part by increasing apoptotic parameters and DNA fragmentation.[17] Furthermore, as shown in other studies.[17–20], curcumin enhanced the effects of other medications and cytokines on bladder cancer cells.

Carotenoids

Carotenoids, which are present in almost all vividly colored fruits, vegetables, and seafood, have potent anti-cancer capabilities, much like curcumin. Their ability to prevent cancer

stems from their antioxidative qualities. Free radicals are chemicals that aim to damage DNA and cell membranes; antioxidants shield cells from these harmful agents. Contrary to popular assumption, not all carotenoids can be turned into vitamin A, even though the carotenoid β-carotene (Figure 1C) has a very high quantity of vitamin A activity. The advantages of carotenoids as antioxidants are numerous. For instance, smokers typically have greater levels of free radicals in because of the toxins they breathe in, their blood. Research indicates that antioxidants could reduce a Lung cancer risk in smokers.[26,27] Additionally, research indicates that carotenoids may aid in the prevention of endometrial cancer[37], prostate, breast, and skin cancers.[27–37, 38, 39] Another carotenoid, astaxanthin (Figure 1D), is present in salmon, red fish, shrimp, and crab and has been shown in rat lung and liver cancer models to exhibit anti-carcinogenic properties. Astaxanthin considerably and dose-dependently reduced the growth of liver cancer cells in the HepG2 human liver cancer cell line.

Polysaccharide

Oranges are orange because of the pigment βcarotene, but they also include GCS-100, a polysaccharide that is generated from oranges and an additional anticancer agent. citrus pectin. GCS100 increases dexamethasone-induced apoptosis and overcomes bortezomib resistance in multiple myeloma cells. Put differently, GCS-100 exhibits anti-angiogenic activity as it reduces the proliferation of multiple myeloma cells and even prevents VEGF-induced cell migration, even in the presence of BMSCs.[40] Additionally, GCS-100 overcomes the cytoprotective effects of the antiapoptotic protein Bcl-2 as well as the growth/survival advantage provided by NF-B. GCS-100-induced biochemical GCS-100 has no effect on mitochondrial apoptotic signaling, which includes changes in DYm, O2- production, or the activation of caspase-9. Instead, apoptosis primarily happens via the caspase-8-to-caspase-3 signaling route. In addition to inhibiting the anti-apoptotic protein Galectin, low dose GCS100 also initiates additive anti-multiple myeloma activity when taken with dexamethasone.[40]

Mushrooms

The mushroom is another natural component that has the potential to be used as a crude medication due to its anti-tumor, antiviral, and antibacterial qualities.

whole spleen cells, macrophages, or NK cells.

These findings imply that higher consumption of White button mushrooms have the potential to strengthen innate immunity against viruses and malignancies by boosting NK cell activity,

which is mediated by elevated TNF-α and IFN-γ production.[43, 44] It is believed that mushrooms have these effects because of their capacity to alter immune cell activities.[43]

These substances are primarily classified as polysaccharides, particularly beta-dglucan derivatives, proteoglycans, proteins, and triterpenoids. They also fall under the category of glycopeptide/protein complexes, or polysaccharide-peptide/protein complexes. Beta (1-->3)-dglucans and their peptide/protein derivatives are among the polysaccharidesand additional proteins: fungal immunomodulatory proteins (Fips) play a significant part in the anti-tumor and immunomodulatory actions.[44, 45]

Resveratrol

Resveratrol (Figure 1E) is another potential crude drug or crude drug element that has been identified based on its capacity to suppress cyclooxygenase (COX) activity that is present in the skin of red grapes and, consequently, in red wine. Cellular processes linked to the development, propagation, and initiation of tumors are inhibited by resveratrol. Moreover, it inhibits the activation of TNF-α The nuclear transcription factors NF-B, AP-1, and apoptosis have been linked to a possible reduction in oxidative stress and lipid peroxidation.[46–48]

Green Tea

Similar to the resveratrol found in grape skins, most people are now aware of the health benefits of green tea. Polyphenols in green tea (-)-Epigallocatechin-3-gallate (EGCG) (Figure 1F) exhibits a number of advantageous characteristics, such as anticarcinogenic, antioxidant, and chemopreventive effects.[49] The potential for EGCG to induce cancer cells to die similarly to healthy cells is one of its advantages. According to a recent study, the JNK-mediated signalingpathway's MAPKKK protein MEKK1 also promotes NF-κB by activating IKKβ. EGCG prevented NF-κB and CREB from binding to DNA in a tumor promoter 12–O-tetradecanoylphorbol-13-acetate (TPA). Mouse skin in living things, In addition, EGCG inhibited TPA-induced phosphorylation of IκBα and its subsequent degradation, as well as p65's nuclear translocation.[53] It has been documented that EGCG inhibits p38 and NF-κB activation, at least in part, to regulate the expression of monocyte chemotactic protein-1 (MCP-1) in endothelial cells, hence having an anti-inflammatory impact.[54] It has been demonstrated that EGCG is beneficial in controlling the mast-cell-mediated allergic inflammatory response by preventing the production of TNF-α, IL-6, and IL-8 by blocking intracellular Ca2+ levels, ERK1/2, and activation of NF-κB.[55] The degradation of IL-1β-receptor-associated kinase (IRAK) induced by EGCG was significantly reduced, as were the

signaling processes that follow IRAK degradation, including NF-κB activation, IKK activation, and I ‡ Bα degradation. Furthermore, EGCG prevented the phosphorylation of the NF-κB p65 subunit. The inhibition of IL-8 gene expression demonstrated the functional impact of this inhibition.[56]

Herbals

Prostate cancer is being studied as a potential treatment for Scutellariabaicalensis, a popular Chinese herbal remedy that has traditionally been utilized as an anti-inflammatory and anticancer agent. Growth inhibition was measured in two human prostate cancer cell lines (PC-3, an androgen-independent line, and LNCaP, an androgen-dependent line) after they were treated to S. baicalensis. In both cell lines, S. baicalensis demonstrated enhanced growth inhibition that was dependent on both time and dose. Following S. baicalensis treatment, PGE2 generation was markedly decreased in both cells; this was due to direct inhibition of COX-2 activity as opposed to COX-2 protein suppression. Moreover, S. baicalensis prevented LNCaP cells from producing prostate-specific antigens. Lastly, S. baicalensis inhibited cdk1 expression and kinase activity in PC-3 cells, which ultimately led to a G2/M cell cycle arrest, and suppressed cyclin D1 expression in LNCaP cells, resulting in a G1 phase arrest. According to animal research, S. baicalensis treatment reduced tumor volume by 50% after 7 weeks, suggesting that the plant may be a new anticancer treatment for prostate cancer.[58] In traditional Asian medicine, Artemisia asiatica has also been widely utilized to treat conditions involving microbial infection, inflammation, and cancer.

Table 1: Crude drugs or elements of crude drugs in various research and clinical phase.

Crude drugs	status	target
Paclitaxel	In FDA-approved clinical use	β-tubulin
Curcumin	In Phase I/II clinical trials	Multiple target
Citrus pectin	In pre-clinical research phase	NF-κB
Mushroom	In pre-clinical research phase	CD4 ,CD8, CD25, IFN-γ, IL-6, TNF-α
Astaxanthin	In pre-clinical research phase	p21CIP1/WAF , GADD153, c-myc
Resveratrol	In pre-clinical research phase	NF-κB
Capsaicin	In pre-clinical research phase	Bcl-2

CONCLUSION

A selection of promising natural ingredients are shown in the preceding excerpts, such as Paclitaxel (Taxol), curcumin, β-carotene, astaxanthin, citrus pectin, mushrooms, and resveratrol. The following substances are being utilized and studied as crude medications or components of crude drugs in research and clinical settings: EGCG, Scutellariabaicalensis,

Artemisia asiatica, red and white ginseng extracts, isoliquiritigenin, and capsaicin (Table 1). Crude medicines may be useful therapeutic targets for cancer because of their diverse effects on oncogenes, cell signaling, and apoptosis (p21CIP1/WAF1, GADD153, c-myc, COX-2, NF-κB, CDK1, p38, and Bcl-2, among others). These are not brand-new medications.

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