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MODERN AND HERBAL MEDICINE IN THE TREATMENT OF CANCER: A REVIEW"

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ABSTRACT

Recent statistics indicate that the overall cancer incidence globally, in spite of billions of dollar spent on research in each year, has not changed significantly in the last half – century. Cancer begins when cells in a part of the body start to grow out of control. There is various type of cancer, but they all start because of out-of-control growth of abnormal cells. Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in 21st century. Cancer is the second leading cause of death in the United States. Allopathic medicine commonly practiced currently is only 100 years old. Although traditional medicine has been around for thousands of years, no integration exists between it and allopathic medicine. The main objective of this review is to identify the available cancer treatments and their possible therapeutic and adverse effects and to highlight the role of herbal medicine in the treatment of cancer which can be a basis of a search of new herbal isolated modern medicine. Ayurveda, the science of long life and one of the most ancient medical system and still practiced on the Indian subcontinent can be used in the combination of modern medicine to provide better treatment of cancer.

KEYWORDS: Chemotherapy, folk medicine, apoptosis, carcinogens, targeted therapy.

1.1 INTRODUCTION

Although cancer is an ancient disease that afflicts humans and other animals, its prominence in the Western world rose from the nineteenth century to become "a disease of civilization." The World Health Organization stated: "World Cancer Report provides clear evidence that

action on smoking, diet and infections can prevent one third of cancers, another third can be cured." Is this cautious optimism warranted?

Cancer begins when cells in a part of the body start to grow out of control or it is the term used when abnormal cells divide without control and are able to invade other tissues.[1] There are various type of cancer, but they all start because of out-of- control growth of abnormal cells. Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in 21st century. Additionally, cancer is a highly complex disease whose development may take as many as 20 to 30 years before it can be detected. Metastasis is a process of travel or spread of cancer cell to other parts of the body.

Cancer cells often spread via three main ways

1- Local spread: cancer cells grow directly into nearby body tissues.

2- Through the blood circulation: cancer cells break way from the primary tumour and then Slip through the walls of blood vessels into through stream until they get stuck Somewhere. Most cancer cells spreading via blood circulation are killed by white cells in the immune system, but some of them stick to platelets to form clumps and give themselves protection, these cells will survive and form metastasis.

3- Through the lymphatic system: cancer cells travel in lymph fluid until they get stuck in small channels inside the lymph node and grow into secondary cancer (metastasis).[2,3]

Secondary cancer doesn't take the characteristics of the cells in the new location, but continue to resemble the primary cancer. A majority of cancers start at a single site in the body and spread to other parts.[4] Technological advances and the increasing understanding of cancer make this field one of the most rapidly evolving areas of modern medicine. However , herbal remedies are believed by the general public to be safe, causes less side-effects and less likely to cause dependency.[5] Ayurveda, a traditional Indian medicine of plant drugs has been successful from very early times in using these natural drugs and preventing or suppressing various tumours using various lines of treatment. For example, Hartwell[6–14] has collected data on about 3000 plants, those of which possess anticancer properties and subsequently been used as potent anticancer drugs.[15] Chemotherapy combined with Chinese herbal medicine is more effective compared with chemotherapy alone. We identified 2 studies that used the exact same herbal formula (Hua Chan Su) and

conducted a separate meta-analysis.[1] Although modern science has made some major strides in understanding cancer and its molecular basis, the knowledge about how to prevent or treat cancer is still lagging behind. Although interruption of a cell signaling pathway, also called monotherapy, has been the paradigm approach until now, experience in the last few years has revealed that multi targeted therapy has a better chance for success.

Epidemiological studies have shown that a diet rich in plant-derived foods is consistently associated with a reduced risk of developing chronic diseases. A common and important guideline from the American Cancer Society, the American Heart Association and the American Diabetes Association to prevent these diseases is to increase the consumption of plant-derived foods and to eat at least five servings of a variety of vegetables and fruits daily.[16] Although it is not clear which compounds in plant foods are responsible for this preventive effect, evidence suggests that flavonoids may participate in this activity. Flavonoids comprise a large group of plant secondary metabolites characterized by a diphenylpropane structure (C6-C3-C6). They are widely distributed throughout the plant kingdom and are commonly found in fruits, vegetables and certain beverages. Numerous preclinical and some clinical studies suggest that flavonoids have potential for the prevention and treatment of several diseases. Some epidemiological studies support a protective role of diets rich in foods with flavonoids and a reduced risk of developing cancer and cardiovascular diseases.[17-22]

According to the WHO survey 80% populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs. Exploration of the chemical constituents of the plants & pharmacological screening may provide us the basis for developing the leads for development of novel agents. In addition, herbs have provided us some of the very important life saving drugs used in the armamentarium of modern medicine. However among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity and about 15% have been investigated phytochemically.[23,24] This shows a need for planned activity guided phytopharmacological evaluation of herbal drugs.

1.2. Modern treatment in cancer

1.2.1. Surgery

Ancient physicians and surgeons knew that cancer would usually come back after it was surgically removed. The Roman physician Celsus wrote, “After excision, even when a scar has formed, none the less the disease has returned.” Galen was a 2nd-century Roman doctor

whose books were preserved for centuries. He was thought to be the highest medical authority for over a thousand years. Galen viewed cancer much as Hippocrates had, and his views set the pattern for cancer management for centuries: he considered the patient incurable after a diagnosis of cancer had been made. Even though medicine progressed and flourished in some ancient civilizations, there was little progress in cancer treatment. The approach to cancer was Hippocratic (or Galenic) for the most part. To some extent the belief that cancer cannot be cured has persisted even into the 21st century. This has served to fuel the fear people have of the disease. Some people, even today, consider all cancer incurable and put off seeing a doctor until it is too late for optimal treatment. Cancer treatment has gone through a slow process of development. The ancients recognized that there was no curative treatment once a cancer had spread, and that intervention might be more harmful than no treatment at all. Galen did write about surgical cures for breast cancer if the tumor could be completely removed at an early stage. Surgery then was very primitive with many complications, including blood loss. It wasn't until the 19th and early 20th centuries that major advances were made in general surgery and cancer surgery. There were great surgeons before the discovery of anaesthesia. John Hunter, Astley Cooper, and John Warren achieved lasting acclaim for their swift and precise surgery.

But when anaesthesia became available in 1846, the work so rapidly advanced that the next hundred years became known as "the century of the surgeon." Three surgeons stand out because of their contributions to the art and science of cancer surgery: Bilroth in Germany, Handley in London, and Halsted in Baltimore. Their work led to "cancer operations" designed to remove the entire tumor along with the lymph nodes in the region where the tumor was located. William Stewart Halsted, professor of surgery at Johns Hopkins University, developed the radical mastectomy during the last decade of the 19th century. His work was based in part on that of W. Sampson Handley, the London surgeon who believed that cancer spread outward by invasion from the original growth. (The general concept of the radical mastectomy can be traced all the way back to Lorenz Heister, a German who wrote about his ideas for mastectomy and lumpectomy in his book, Chirurgie, published in 1719.).

Halsted did not believe that cancers usually spread through the bloodstream: "Although it undoubtedly occurs, I am not sure that I have observed from breast cancer, metastasis which seemed definitely to have been conveyed by way of the blood vessels." He believed that adequate local removal of the cancer would cure it — if the cancer later appeared elsewhere,

it was a new process. That belief led him to develop the radical mastectomy for breast cancer. This became the basis of cancer surgery for almost a century. Then, in the 1970s, modern clinical trials demonstrated that less extensive surgery is equally effective for most women with breast cancer. Today, a radical mastectomy is almost never done and the "modified radical mastectomy" is performed less frequently than before. Most women with breast cancer now undergo local removal of the primary tumour (lumpectomy) followed by radiation therapy. At the same time Halsted and Handley were developing their radical operations, another surgeon was asking, "What is it that decides which organs shall suffer in a case of disseminated cancer?" Stephen Paget, an English surgeon, concluded that cancer cells spread by way of the bloodstream to all organs in the body but were able to grow only in a few organs. In a brilliant leap of logic he drew an analogy between cancer metastasis and seeds that "are carried in all directions, but they can only live and grow if they fall on congenial soil." Paget's conclusion that cells from a primary tumor spread through the bloodstream but could grow only in certain, and not all, organs was an accurate and highly sophisticated hypothesis that was confirmed by the techniques of modern cellular and molecular biology almost a hundred years later. This understanding of metastasis became a key element in recognizing the limitations of cancer surgery. It eventually allowed doctors to develop systemic treatments used after surgery to destroy cells that had spread throughout the body and use less mutilating operations in treating many types of cancer. Today these systemic treatments may also be used before surgery. During the final decades of the 20th century, surgeons developed greater technical expertise in minimizing the amounts of normal tissue removed during cancer operations. Like the trend from radical mastectomy to lumpectomy, progress was also made in removing bone and soft tissue tumours of the arms and legs without the need for amputation in most cases, and in avoiding a colostomy for most patients with rectal cancer. This progress depended not only on understanding cancer better as a disease and on better surgical instruments, but also on combining surgery with chemotherapy and/or radiation. Until the end of the 20th century, diagnosing cancer required "exploratory surgery" to open the abdomen (belly) or chest so the surgeon could take tissue samples to be tested for cancer. Starting in the 1970s, progress in ultrasound (sonography), computed tomography (CT scans), magnetic resonance imaging (MRI scans), and positron emission tomography (PET scans) have replaced most exploratory operations. CT scans and ultrasound can also be used to guide biopsy needles into tumours. Today, doctors use instruments with fiberoptic technology and miniature video cameras to look inside the body. Surgeons can operate using special surgical instruments through narrow tubes put into small

cuts in the skin. This is called endoscopic surgery, and it can be used to remove tumours in the colon, oesophagus, or bladder. Similar instruments can also be used to look and work inside the abdomen (laparoscopic surgery) or chest (thorascopic surgery). Less invasive ways of destroying tumours without removing them are being studied and/or used. Cryosurgery (also called cryotherapy or cryoablation) uses liquid nitrogen spray or a very cold probe to freeze and kill abnormal cells. Lasers can be used to cut through tissue (instead of using a scalpel) or to vaporize (burn and destroy) cancers of the cervix, larynx (voice box), liver, rectum, skin, and other organs. Radiofrequency ablation transmits radio waves to a small antenna placed in the tumour to kill cancer cells by heating them. Surgery is the main treatment for kidney cancer that has not yet spread. One technique that surgeons are using more often is laparoscopy. For this technique, the surgeon makes several small incisions in the abdomen to insert a tiny light, a camera, and instruments used to view and remove the tumour. This type of surgery has been shown to be just as effective as traditional surgery and easier to recover from. If cancer has spread beyond the kidneys, it is usually treated with surgery. A number of large studies of metastatic kidney cancer have shown that people whose tumours are removed live longer than those whose tumours are not removed.

1.2.2. Hormone therapy

Another 19th century discovery laid the groundwork for an important modern method to treat and prevent breast cancer. Thomas Beatson graduated from the University of Edinburgh in 1874 and developed an interest in the relation of the ovaries to milk formation in the breasts. In 1878 he discovered that the breasts of rabbits stopped producing milk after he removed the ovaries. He described his results to the Edinburgh Medico-Chirurgical Society in 1896: "This fact seemed to me of great interest, for it pointed to one organ holding control over the secretion of another and separate organ." Because the breast was "held in control" by the ovaries, Beatson decided to test removal of the ovaries (called oophorectomy) in advanced breast cancer. He found that oophorectomy often resulted in improvement for breast cancer patients. He also suspected that "the ovaries may be the exciting cause of carcinoma" of the breast. He had discovered the stimulating effect of the female ovarian hormone (estrogen) on breast cancer, even before the hormone itself was discovered. His work provided a foundation for the modern use of hormone therapy, such as tamoxifen, to treat or prevent breast cancer. A half century after Beatson's discovery, Charles Huggins, a urologist at the University of Chicago, reported dramatic regression of metastatic prostate cancer after the testicles were removed. Later, drugs that blocked male hormones were found to be effective

treatment for prostate cancer. Today these drugs are being studied to determine if they have a role in preventing prostate cancer. New classes of drugs (such as aromatase inhibitors, LHRH [luteinizing hormone releasing hormone] analogues and inhibitors, and others) have greatly changed the way prostate and breast cancers are treated. Research to better understand how hormones influence cancer growth has guided progress in developing many new drugs for cancer treatment. It is also helping researchers look at new ways to use drugs to reduce the risk of developing breast and prostate cancer.

1.2.3. Radiation

In 1896 a German physics professor, Wilhelm Conrad Roentgen, presented a remarkable lecture entitled "Concerning a New Kind of Ray." Roentgen called it the "X-ray", with "x" being the algebraic symbol for an unknown quantity. There was immediate worldwide excitement. Within months, systems were being devised to use x-rays for diagnosis, and within 3 years radiation was used in to treat cancer. In France, a major breakthrough took place when it was discovered that daily doses of radiation over several weeks greatly improved the patient's chance for a cure. The methods and the machines that deliver radiation therapy have steadily improved since then. Today, radiation is delivered with great precision to destroy cancer tumours while limiting damage to nearby normal tissues. At the beginning of the 20th century, shortly after radiation began to be used for diagnosis and therapy, it was discovered that radiation could cause cancer as well as cure it. Many early radiologists used the skin of their arms to test the strength of radiation from their radiotherapy machines, looking for a dose that would produce a pink reaction (erythema) which looked like sunburn. They called this the "erythema dose," and this was considered an estimate of the proper daily fraction of radiation. It is no surprise that many of them developed leukaemia from regularly exposing themselves to radiation. Advances in radiation physics and computer technology during the last quarter of the 20th century made it possible to aim radiation more precisely. Conformal radiation therapy (CRT) uses CT images and special computers to very precisely map the location of a cancer in 3 dimensions. The patient is fitted with a plastic mold or cast to keep the body part still. The radiation beams are matched to the shape of the tumour and delivered to the tumor from several directions. Intensity-modulated radiation therapy (IMRT) is like CRT, but along with aiming photon beams from several directions; the intensity (strength) of the beams can be adjusted. This means that proton beam radiation can deliver more radiation to the cancer while reducing damage to nearby normal tissues.

1.2.3.1. Stereotactic radio surgery

Stereotactic radio surgery and stereotactic radiation therapy are terms that describe several techniques used to deliver a large, precise radiation dose to a small tumour. The term surgery may be confusing because no cut (incision) is actually made. The most common site treated with this radiation technique is the brain. The linear accelerator, or a special machine known as a Gamma Knife, can be used to deliver this treatment. Research is being done to develop delivery systems to treat sites other than the brain.

1.2.3.2. Intra operative radiation therapy

Intraoperative radiation therapy (IORT) is a form of treatment that delivers radiation at the time of surgery. The radiation can be given directly to the cancer or to the adjacent tissues after the cancer has been removed. It is more commonly used in abdominal or pelvic cancers and in cancers that tend to recur (come back after treatment). IORT minimizes the amount of tissue that is exposed to radiation because normal tissues can be moved out of the way during surgery and shielded, allowing a higher dose of radiation to the cancer.

1.2.4. Chemotherapy

During World War II, naval personnel who were exposed to mustard gas during military action were found to have toxic changes in the bone marrow cells that develop into blood cells. During that same period, the US Army was studying a number of chemicals related to mustard gas to develop more effective agents for war and also develop protective measures. In the course of that work, compound called nitrogen mustard was studied and found to work against a cancer of the lymph nodes called lymphoma. This agent served as the model for a long series of similar but more effective agents (called alkylating agents) that killed rapidly growing cancer cells by damaging their DNA. Not long after the discovery of nitrogen mustard, Sidney Farber of Boston demonstrated that aminopterin, a compound related to the vitamin folic acid, produced remissions in children with acute leukaemia. Aminopterin blocked a critical chemical reaction needed for DNA replication. That drug was the predecessor of methotrexate, a cancer treatment drug used commonly today. Since then, other researchers discovered drugs that block different functions in cell growth and replication. The era of chemotherapy had begun. Metastatic cancer was first cured in 1956 when methotrexate was used to treat a rare tumour called choriocarcinoma. Over the years, chemotherapy drugs (chemo) have successfully treated many people with cancer. Today, several approaches are being studied to improve the activity and reduce the side effects of chemo. These include:

- New drugs, new combinations of drugs, and new delivery techniques.
- Novel approaches to using drugs targeted more specifically at the cancer cells (such as liposomal therapy and monoclonal antibody therapy) to produce fewer side effects.
- Drugs to reduce side effects, like colony-stimulating factors, chemoprotective agents (such as dexrazoxane and amifostine), and anti-emetics (to reduce nausea and vomiting)
- Agents that overcome multi-drug resistance.

1.2.4.1 Liposomal therapy

Liposomal therapy is a new technique that puts chemo drugs inside liposomes (synthetic fat globules). The liposome, or fatty coating, helps them penetrate the cancer cells more selectively and decreases possible side effects (like hair loss, nausea, and vomiting). Examples of liposomal drugs are Doxil (the encapsulated form of doxorubicin) and Daunoxome (the encapsulated form of daunorubicin). Early in the 20th century, only cancers small and localized enough to be completely removed by surgery were curable. Later, radiation was used after surgery to control small tumor growths that were not surgically removed. Finally, chemotherapy was added to destroy small tumor growths that had spread beyond the reach of the surgeon and radiotherapist. Chemo used after surgery to destroy any remaining cancer cells in the body is called adjuvant therapy. Adjuvant therapy was tested first in breast cancer and found to be effective. It was later used in colon cancer, testicular cancer, and others. A major discovery was the advantage of using multiple chemotherapy drugs (known as combination chemotherapy) over single agents. Some types of very fast-growing leukaemia and lymphoma (tumours involving the cells of the bone marrow and lymph nodes, respectively) responded very well to combination chemo, and clinical trials led to gradual improvement of the drug combinations used. Many of these tumours can be cured today by appropriate combination chemotherapy.

1.2.5 Immunotherapy

Better understanding of the biology of cancer cells has led to the development of biologic Agents that mimic some of the natural signals that the body uses to control cell growth.

Clinical trials have shown that this cancer treatment, called biological response modifier (BRM) therapy, biologic therapy, biotherapy, or immunotherapy, is effective for several Cancers. Some of these biologic agents, which occur naturally in the body, can now be made in the lab. Examples are interferon, interleukins, and other cytokines. These agents are given

to patients to imitate or influence the natural immune response. They do this either by directly altering the cancer cell growth or by acting indirectly to help healthy cells control the cancer. One of the most exciting applications of biologic therapy has come from identifying certain tumour targets, called antigens, and aiming an antibody at these targets. This method was first used to find tumours to diagnose cancer and more recently has been used to attack cancer cells. Using technology that was first developed during the 1970s, scientists can mass produce monoclonal antibodies that are specifically targeted to chemical components of cancer cells. Refinements to these methods, using recombinant DNA technology, have improved the effectiveness and decreased the side effects of these treatments. The first therapeutic monoclonal antibodies, rituximab (Rituxan) and trastuzumab (Herceptin) were approved during the late 1990s to treat lymphoma and breast cancer, respectively. Medications are used to increase the body's natural ability to fight cancer. Two such drugs—interleukin-2 (Proleukin) and interferon alfa (Intron A, Roferon-A)—can cause some kidney tumours to shrink by more than half. However, immunotherapy works in only 10 percent to 15 percent of patients. Still, in about 5 percent to 10 percent of people with kidney cancer, interleukin-2 can lead to a long-term remission of metastatic cancer. In some cases the tumours even disappear, and people have lived more than 20 years after their kidney cancer diagnosis. Researchers are trying to find ways to identify those patients most likely to benefit from immunotherapy. Immunotherapy is often combined with newer medications called targeted treatments.

1.2.6 Targeted therapy

Today, three targeted treatments are approved for people with metastatic kidney cancer: sorafenib (Nexavar), sunitinib (Sutent), and temsirolimus (Torisel).

Sorafenib (Nexavar) Sorafenib was approved by the U.S. Food and Drug Administration (FDA) in 2005 to treat metastatic kidney cancer. It can be taken in pill form. Sorafenib has been shown to shrink kidney tumours in many people who have already tried other treatments that didn't work. In a study of more than 900 people with kidney cancer, sorafenib shrank kidney tumors in about 80 percent of patients. In addition, it was very effective in slowing tumour growth. Common side effects of the medication, such as loose stools, are generally easy to treat. Sorafenib as well as sunitinib, discussed below, takes advantage of one of the things we know about how kidney tumours grow. Much like normal tissues, tumours need to have a blood supply. Blood vessels grow in several ways. One way is through the presence of

proteins called vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF). These proteins stimulate blood vessels to grow into tumours. When tumour cells spread through the body, they release VEGF and PDGF to create new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumour. Sorafenib works by stopping VEGF and PDGF from stimulating the growth of new blood vessels in tumors. Because normal tissues have an established blood supply, they are not affected by the medication. Sunitinib (Sutent) In 2006, the FDA approved sunitinib for treatment of metastatic kidney cancer. Like sorafenib, sunitinib is a pill that can be taken by mouth. It is taken once a day for four weeks, followed by a two-week break, then another four week cycle. In clinical trials comparing sunitinib with the immunotherapy interferon, sunitinib was shown to stop the growth of metastatic kidney tumours for twice as long as interferon. Because it is so effective, sunitinib is often used as a first treatment for metastatic kidney cancer. Researchers also have shown that sunitinib can shrink kidney tumours in many people who have already tried other treatments that did not work.

1.2.7 Growth signal inhibitors

Growth factors are hormone-like substances that help tell cells when to grow and divide. Their role in fetal growth and repair of injured tissue was first recognized in the 1960s. Later it was realized that abnormal forms or abnormally high levels of the same factors contribute to the growth and spread of cancer cells. Researchers have also started to understand how cells recognize these factors, and how that recognition leads to signals inside the cells that cause the abnormal features of cancer cells. Changes in these signal pathways have also been identified as a cause of the abnormal behaviour of cancer cells. During the 1980s, scientists found that many of the growth factors and other substances responsible for growth factor recognition and signalling are actually products of oncogenes. Among the earliest targeted therapies that block growth signals are trastuzumab (Herceptin), gefitinib (Iressa), imatinib (Gleevec), and cetuximab (Erbitux).Current research has shown great promise for these treatments in some of the more difficult to treat and deadly forms of cancer, such as non-small cell lung cancer, advanced kidney cancer, and glioblastoma. And second generation targeted therapies, like dasatinib (Sprycel) and nilotinib (Tasigna), have already been found to produce faster and stronger responses in certain types of cancer and were better tolerated.

1.2.8 Angiogenesis inhibitors

Angiogenesis is the creation of new blood vessels. The term comes from 2 Greek words: angio, meaning "blood vessel," and genesis, meaning "beginning." Normally, this is a healthy process. New blood vessels, for instance, help the body heal wounds and repair damaged tissues. But in a person with cancer, this same process creates new, very small blood vessels that give a tumour its own blood supply and allow it to grow. Anti-angiogenesis is a form of targeted therapy that uses drugs or other substances to stop tumours from making the new blood vessels they need to continue growing. This concept was first proposed by Judah Folkman in the early 1970s, but it wasn't until 2004 that the first angiogenesis inhibitor, bevacizumab (Avastin), was approved for clinical use. Currently used to treat advanced colorectal, kidney, and lung cancers, bevacizumab is being studied as treatment for many other types of cancer, too. And many new drugs that block angiogenesis have become available since this first one in 2004.

1.2.9 Apoptosis-inducing drugs

Apoptosis is a natural process through which cells with DNA too damaged to repair – such as cancer cells – can be forced to die. Many anti-cancer treatments (including radiation and chemo) cause cell changes that eventually lead to apoptosis. But targeted drugs in this group are different, because they are aimed specifically at the cell substances that control cell survival and death. Of the more than 75 'Treatments for Cancer' that emerged in this study, six 'Treatment' codes were among the top ten most frequently mentioned treatments for both the Healer and the SR groups. These six 'Treatment' codes are as follows2:

- Treatment: Spiritual: Achieving a Transcendent State or a Deepening of Spirituality
- Treatment: Mental/Emotional: Trusting in Intuition
- Treatment: Mental/Emotional: Releasing Negative and/or Repressed Emotions
- Treatment: Mental/Emotional: Feeling Love/Joy/Happiness
- Treatment: Physical: Diet Change
- Treatment: Physical: Herbs or Vitamins

Note: These six codes are listed in the order suggested by a sub-theme that was discussed in the 'Underlying Beliefs' section, such that spiritual treatments are listed first, mental/emotional treatments are listed second, and physical treatments are listed last. However, this order was chosen for organizational purposes only; it is important to note that all six treatments were equally frequent among both groups of participants.

1.2.9.1 Achieving a transcendent state, or a deepening of spirituality.

The first code, "Treatment: Spiritual: Achieving a transcendent state, or a deepening of spirituality" was applied whenever a subject described achieving a transcendent state, or deepening his/her connection with a higher spiritual force/energy in order to help remit cancer.

Both healers and SR subjects discussed this code frequently.

We would define it [Spontaneous Remission] more in terms of a spiritual connection and in our system you're an active participant. So you are connecting yourself to these forces that exist and are made possible for you to use for yourself.

1.2.10 Classifications of anticarcinogens

Several classifications of the mechanisms of anticancer agents have been proposed by a number of investigators.[25] Subdivided anticarcinogens into two major categories; blocking agents and suppressing agents on the basis by which they exert protective effect at specific stages of multi-step carcinogenesis. Blocking agents are substances that can inhibit initiation either by inhibiting the formation of carcinogens from precursor molecules or reactive intermediates from the parent carcinogens, or by preventing the ultimate electrophilic species from interacting with macromolecules such as DNA, RNA and proteins. Suppressing gents act at the promotion or the progression stage by preventing the malignant expression of initiated cells. Some classifications of anticarcinogens distinguish inhibitors based on their intervention level throughout the process leading from a normal cell to an initiated cell, and then to dysplasia of increasing severity up to carcinoma in situ, and ultimately to cancer[26,27] presented a detailed classification of mechanisms of inhibitors of mutagenesis and carcinogenesis. A revised and updated classification was also proposed recently.[28] Accordingly, the classification took into consideration the multiple phases involved in the pathogenesis of cancer related diseases. It analyzed first the inhibition of mutation and of cancer initiation, either extracellular or inside the cells and then the mechanisms interfering with promotion, progression, invasion and metastasis. A modified scheme incorporating possible points of intervention.

Flavonoids are characterized by a molecular frame of two phenyl rings linked by a three carbon chain, making them good electron donators or acceptors. Their anti-oxidant capacity depends on this framework, the number and pattern of substitutions (primarily with hydroxyl

groups), their ability to chelate with metal ions, and on their specific environment. Anti-oxidant properties of a specific substance are complex, and relative efficacies of two substances can vary in different test assays.[29,30] A more comprehensive review of luteolin as an anti-oxidant, radical-scavenging and anti-inflammatory agent is published separately in a related paper.[31] Briefly, the ortho-dihydroxy structure in the B-ring and the 2,3-double bond in conjugation with the 4-oxo function of the C-ring provides a good, but not excellently high anti-oxidant capacity of luteolin. In cell-free tests, luteolin is usually inferior to quercetin which has an additional hydroxyl substitution in position 3 . However, it is more lipophilic and may perform better in test systems with biological molecules or membranes. Luteolin can form chelates with metal ions, but is again less active in this Molecules 2008, 13 2630 respect than quercetin.[32] However, it is not oxidized during the chelation process. This may explain why luteolin does not undergo redox cycling as do quercetin and other flavonols, a process increasing their potential to act as pro-oxidants with possible deleterious effects. Nevertheless, although structure activity relationship studies are a helpful tool to predict biological activities, experiments have to be carried out under physiological conditions for a final proof. In plants, many flavonoids are found in the form of glycosides but they are cleaved to their aglycones in the intestinal mucosa, and the aglycones are degraded or glucuronated by UDP glucuronosyl transferases before release into blood serum[33] Wittemer et al.[34] investigated pharmacokinetics of aqueous artichoke extracts containing luteolin-7-O-glucoside in humans. Neither luteolin nor its glucosides were found in urine or plasma, but only their phase II-conjugates. Anti-oxidant properties are to a large extent attributable to hydroxylation in positions 3' and 4'; it is there, where flavonoids are preferentially glucuronidized during resorption in the gut.[35] This might reduce the flavonoids' anti-oxidant potential. However, several human tissues and cell lines, e.g., neutrophile granulocytes and CaCo-2 cells, are able to cleave luteolin glucuronides, and increase their activity when stimulated by pro-inflammatory substances.[36]

In vivo skin penetration studies of the flavones apigenin, luteolin, and apigenin-7-O-β-glucoside with human volunteers showed that except of the glucoside they were not only adsorbed at skin surface, but penetrated into deeper skin layers. This is important for their topical use as antiphlogistic agents in dermatology.[37]

Anti-cancer-strategies include protection of tissue from carcinogenic stimuli, suppression of procarcinogenic regulatory mechanisms and cell proliferation, modulation of intercell

communication signals, destruction or removal of tumour cells, and induction of apoptosis. In solid tumours, a further strategy is to inhibit growth of blood vessels which supply and promote the tumour. Luteolin, like a number of other flavonoids and polyphenols[38] displays a variety of pharmacological effects in vitro and in vivo which may contribute to anti-carcinogenic activity provided that effective concentration levels are reached at the target sites under realistic conditions.

2. Cancer drugs are classified into

2.1. Alkylating Agents

Alkylating agents directly damage the DNA and prevent the cancerous cells from replicating, according to the American Cancer Society (ACS). Alkylating agents are used to treat acute and chronic leukemia, ovarian cancer, breast cancer, lung cancer, lymphoma, Hodgkin disease, multiple myeloma and sarcoma. In some patients, alkylating agents can cause long-term damage in the bone marrow; in rare cases, the drugs can cause acute leukemia. Five types of alkylating agents are used to treat cancer: nitrogen mustards (mechlorethamine, chlorambucil, cyclophosphamide, ifosfamide and melphalan), nitrosoureas (streptozocin, carmustin and lomustine), alkyl sulfonates (busulfan), triazines (dacarbazine and temozolomide) and ethylenimines (thiotepa and altretamine).

2.1.2 Antimetabolites

Antimetabolites are another cancer drug option. These interfere with DNA and RNA growth, according to the ACS. Antimetabolites are used to treat leukemias, breast tumors, ovarian tumors and intestinal tract tumors. Examples of antimetabolites are 5-fluorouracil, capecitabine, 6 mercaptopurine, methotrexate, gemcitabine, cytarabine, fludarabine and pemetrexed.

2.1.3. Anthracyclines

Anthracyclines are anti-tumor antibiotics that disrupt DNA replication by interfering with enzymes; anthracyclines treat a variety of cancers. If patients are given high doses of anthracyclines, heart damage can occur. Types of anthracyclines used to treat cancer include daunorubicin, doxorubicin, epirubicin and idarubicin.

2.1.4. Topoisomerase Inhibitors

Topoisomerase inhibitors also prevent DNA replication of the cancer cells by interfering with the enzyme topoisomerase. Leukemia, lung cancer, ovarian cancer and gastrointestinal cancer

can be treated with topoisomerase inhibitors. Two types of topoisomerase inhibitors exist: topoisomerase I inhibitors (topotecan and irinotecan) and topoisomerase II inhibitors (etoposide and teniposode).

2.1.5. Mitotic Inhibitors

Mitotic inhibitors work by either stopping mitosis or prohibiting protein production, according to the ACS. Mitotic inhibitors treat breast cancer, lung cancer, myelomas, lymphomas and leukemias. However, mitotic inhibitors can cause peripheral nerve damage in some patients. Examples of mitotic inhibitors are taxanes (paclitaxel and docetaxel), epothilones (ixabepilone), vinca alkaloids (vinblastine, vincristine and vinorelbine) and estramustine.

2.1.6. Corticosteroids

Corticosteroids are cancer drugs that act as either an anti-emetic medication or a chemotherapy medication. For example, the corticosteroids prevent nausea, vomiting and allergic reactions of chemotherapy. Corticosteroids also slow the growth of cancer cells in lymphoma, leukemias and multiple myeloma. Prednisone, methylprednisolone and dexamethasone are all types of corticosteroids used in cancer treatment.

2.1.7. Aromatase

Aromatase is an enzyme that plays a critical role in the development of estrogen receptor positive breast cancer. As aromatase catalyzes the aromatization of androstenedione to estrone, a naturally occurring estrogen, it is a promising drug target for therapeutic management. The undesirable effects found in aromatase inhibitors (AIs) that are in clinical use necessitate the discovery of novel AIs with higher selectivity, less toxicity and improving potency. In this study, we elucidate the binding mode of all three generations of AI drugs to the crystal structure of aromatase by means of molecular docking. It was demonstrated that the docking protocol could reliably reproduce the interaction of aromatase with its substrate with an RMSD of 1.350 Å. The docking study revealed that polar (D309, T310, S478 and M374), aromatic (F134, F221 and W224) and non-polar (A306, A307, V370, L372 and L477) residues were important for interacting with the AIs. The insights gained from the study herein have great potential for the design of novel AIs. Many drugs used for the treatment of estrogen receptor-positive breast cancer are mechanistically based on interfering with either estrogen production or estrogen action. Cytochrome P450 19A1 (CYP19A1; EC 1.14.14.1), commonly known as aromatase, is an enzyme located in the endoplasmic

reticulum of estrogen-producing cells that functions in the conversion of androgens to estrogens. It is comprised of a polypeptide chain of 503 amino-acid residues and a prosthetic heme group at its active site. An androgen-specific cleft consisting of hydrophobic and polar residues is situated within the confinement of the aromatase binding site. Such cleft is specific androstenedione binding to catalyze androgen to estrogen via a three-step process. Each step requires one mol of O2, one mol of NADPH and NADPH cytochrome reductase. This reaction converts androstenedione, testosterone and 16α-hydroxytestosterone to estrone, 17β-estradiol and 17β,16α-estriol, respectively.[40] The two initial steps are the typical C19-methyl hydroxylation, while aromatization of the steroid A-ring is catalyzed at the final step. To block estrogens production, it is necessary to inhibit the enzyme through the use of aromatase inhibitors (AIs). AIs are only effective for post-menopausal women since they do not block estrogen production in the ovaries but act only on the local estrogen produced by breast cancer cells. Therefore, AIs serve as front-line therapy for estrogen-dependent breast cancer.[41]

To date, three generations of AIs are available. The first generation of AI is aminoglutethimide that was marketed in the late 1970s. Unfortunately, aminoglutethimide was far from being an ideal drug since it exhibited several drawbacks, most notably high toxicity.[42,43] and lack of selectivity, since it can inhibit other CYP450 enzymes involved in cortisol and aldosterone biosynthesis.[44] Such flaws limited its use and led to its eventual withdrawal from the market. Nevertheless, aminoglutethimide served as the prototype for later AIs with emphasis on developing more potent, selective and less toxic AIs. Continuing on to the second generation, fadrozole (Figure 2), which contains an imidazole group[45], is more selective and potent than aminoglutethimide. Nevertheless, it still displayed effects on aldosterone, progesterone and corticosterone biosynthesis. Formestane[46], a steroid analogue, was the first selective AI used in clinical trial. It was demonstrated to be effective and was well tolerated.[46]

Finally, the third generation of AIs includes two triazole derivatives, anastrozole[47] and letrozole.[48], and one steroid analogue, exemestane.[48] These AIs displayed improved efficacy and lower toxicity as compared with the estrogen antagonist, tamoxifen, in both early and advanced breast cancer.[49,50] For this reason, the last generation of AIs has been recommended by the FDA as first-line drugs for therapy of breast carcinoma. Anastrozole and letrozole, are non-steroid derivatives and competitive inhibitor of androstenedione.

New aromatase inhibitors (AI) (second-generation: formestane and fadrozole; third-generation: letrozole, anastrozole, vorozole, and exemestane) have been tested in several controlled clinical trials after tamoxifen failure in metastatic breast carcinoma (MBC). They have resulted in better survival compared with megestrol acetate (MEG) in a number of studies. The authors performed a pooled analysis including all the Phase III trials published between 1996 and 2004 evaluating the AIs approved or not by the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medical Products (EMEA) as second-line endocrine therapy (ET) for patients with MBC.

The catalytic activity of aromatase is essentially a three-step process involving the conversion of androstenedione and testosterone to estrone and estradiol, respectively.[39] The first two steps entails the hydroxylation of C19-methyl group, which is modulated by three amino acid residues, comprising A306 and T310[51], and two catalytic water molecules which activates the ferrous dioxygen to the hydroxylating Fe(IV) = O form. This is followed by a H2β abstraction of the 2,3-enolization process in the aromatization step that essentially entails a nucleophilic attack on H2β-C by A306 and T310 along with concerted electrophilic attack on C3-keto oxygen by D309 to drive H2β abstraction and 2,3-enolization. Finally, the electrons delocalize to form an aromatic system and estrone and formic acid are released as products. As many cofactors (e.g., H2O, O2 and NADPH) are needed for catalytic activity, its proper entrance into the binding site is essential for catalytic activity. It then follows that decreasing the space within the binding cavity by means of ligand docking may hinder the entrance of cofactors into the cavity resulting in the inhibition of the aromatization process. The occupation of androstenedione within the aromatase binding site leaves a larger empty space within the cavity when compared to the empty space remaining after binding to AIs

4. Herbal Medicine in the Treatment of Cancer

For a long times plants have been provide essential nutritional values, medicinal properties and notable physiological effect to life and are a good source of food.[52] Traditional medicine (TM) refers to the application, approach, knowledge, and belief in incorporating plant or animal based properties in remedies, singularly or in combination, for the purpose of treating or preventing disease as well as to maintain the well-being of an individual. Population rise, inadequate supply of drugs, prohibitive cost of treatments, side effects of several allopathic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide

variety of human ailments.[53] As such herbal remedies have been used to cure a variety of disorders or conditions such as diabetes, cardiovascular problems, weight control, dermal infirmities, sexual malfunction, and of course cancer. According to the World Health Organization, more than 70% of the world's population uses TM in order to fulfill their health necessities.[54] The principles underlying herbal medicines are relatively simple, although they are quite distinct from conventional medicine and herbal medicine.[55] India is a rich source of medicinal plants and a number of plant extracts are used against diseases in various systems of medicine such as ayurveda, unani and siddha. Only a few of them have been scientifically explored. Plant derived natural products such as flavanoids, terpenes, and alkaloids[56-58] and soon has received considerable attention in recent years, due to their diverse pharmacological properties including cytotoxic and cancer chemo preventive effects.[59] The natural world has been providing lifesaving antibiotics, nutritive supplements and our most potent anti-cancer drugs. The lush tropical rainforests and colorful coral reefs of our planet have long been a source of promise in the fight against cancer and other diseases. Natural products, especially those from plants, have been avaluable source of new cancer drugs for many decades. Medicinal plants are the most exclusive source of life saving drugs for the majority of the world's population. The use of plant products in the treatment of cancer has been of recent interest.[60] In the market, these products are offered as "natural products".[61] Cancer is the abnormal growth of cells in our body that can lead to death. Cancer cells usually invade and destroy normal cells. More and more cancer research works have been done and yet we do not understand exactly what cancer is?.[62] Cancer is the second leading cause of death in America. The major cause of cancer is smoking, dietary imbalances, hormones and chronic infections leading to chronic inflammation.[63]

3.1 Allium Sativum

A member of the Liliaceae family, garlic (Allium sativum) is highly regarded throughout the world for both its medicinal and culinary value. . In addition to its reputation as a healthy food, garlic has shown anti-viral, anti-bacterial, antifungals and antioxidant capacities. Additionally, anti-atherosclerotic and anti-cancer properties have also been demonstrated. The genus Allium includes garlic, scallions, onions, chives, and leeks. These contain the sulfur compounds which are medicinally active. Most of the sulfur found in whole garlic cloves are of two types found in equal quantities: the S-alkylcysteine sulfoxides and the γ-glutamyl-S-alkylcysteines. The most abundant sulfur compound in garlic is alliin (S-

allylcysteine sulfoxide), which is present at 10 mg/g in fresh garlic or 30 mg/g dry[64] . Of the many favorable actions of garlic, inhibition of the growth of cancer is perhaps the most notable. Various forms of garlic, including fresh garlic extract, aged garlic, garlic oil and a number of organosulphur compounds, appear to offer protection against some cancers. Garlic likely has several synergestic biological effects that either prevent or possibly may fight cancer. The chemo preventive activity has been attributed to the ability to modulate the activity of several metabolising enzymes that activate (cytochrome P450s) or detoxify (glutathione S-transferases) carcinogens and inhibit the formation of DNA adducts in several target tissues.[65] Also, garlic was shown to stimulate immune effector cells including T- and natural killer cell number and activity. Numerous epidemiological, clinical and laboratory studies have demonstrated the role of garlic in cancer prevention.[66-69] especially in relation to digestive tract cancers, including oesophageal and stomach cancers.[70-71] There is also promising research evaluating the use of garlic in leukemic[65], melanoma[72] and neuroblastoma[73] cell lines.

3.2 Catharanthus roseus

Periwinkle (Catharanthus roseus) is one of the most important medical and ornamental plants in the world. It is one of the very few medicinal plants, which has a long history of uses as diuretic, antidysenteric, hemorrhagic and antiseptic. It is known for use in the treatment of diabetes in Jamaica and India. The alkaloids vinblastine and vincristine present in the leaves are recognized as anticancerous drugs. Vinblastine is used in combination with other anticancer agents for the treatment of lymphocytic lymphoma, Hodgkin's disease - cancer affecting lymph glands, spleen and liver, testicular carcinoma and choriocarcinoma. Vincristine is used in acute leukemia, lymphosarcoma and Wilm's tumour. Vinblastine and

vincristine are primarily used in combination with other cancer chemotherapeutic drugs for the treatment of a variety of cancers, including leukemia's, lymphomas, advanced testicular cancer, breast and lung cancers, and Kaposi's sarcoma.[74]

3.3 Jasminum Angustifolium

Jasminum angustifolium Linn. belonging to the family Oleaceae is distributed in south India (kerala, Karnataka) on the hills of lower elevation. Jasminum angustifolium (Linn.) wild, has very limited systematically carried out investigations. The traditional systems of Siddha and Ayurvedic medicine use this plant alone or in combination with other medicinal plants for the treatment of various diseases. It was found from the tribes of south India that the plant has been used for the suppression of tumour like syndrome among their own population. Jasminum grandiflorum which belongs to the same botanical family is having anticancer activity (especially against Hodgkin's disease, cancer of the bone, lymph nodes, breast and DMBA- induced mammary carcinogenesis)[75,76] The shade dried whole plant of Jasminum angustifolium Linn. Was powdered coarsely and about 750g of this powder was extracted (soxhlet) with 70% ethyl alcohol and aqueous for 72h. The yield was 22.4g w/w and 4.8g w/w respectively. The extract was dried in vacuum and re-suspended in water before use. The Phytochemical screening proves the presence of carbohydrate, glycosides and flavonoids[77,78]

3.4 Annona Squamosa

Annona squamosa (Annonaceae) commonly known as custard apple, is a native of West Indies and is now cultivated throughout India, mainly for its edible fruits.[79] It is a fruit tree, and the seeds are famous to contain many acetogenins, waxy substances, consisting long chain fatty acids, they showed antimalarial , immunosuppressive, antifeedent, antiparasitic, and pesticide, cell growth inhibitory and particularly remarkable cytotoxic activity.[80] Squamocin is another annonaceous acetogenin has been reported to exert antiproliferative effects on HL-60 cancer cells via activation of caspase-3. The preliminary pytochemical screening of this plant revealed a number of alkaloids,terpene derivatives and a normal diazepine,squamolone.[81] Annona squamosa bark was collected in and around Chidambaram, Tamil nadu, India and authenticated by the Botanist, Dr.S.Sivakumar, Department of Botany, Annamali University. A voucher specimen (AU04218) was also deposited. The ethanolic extracts of Annona squamosa bark were prepared according to the method of Hossain et al.[82] Five hundred grams of dried and finely powdered Annona squamosa barks were soaked in 1500 ml of 95% ethanol overnight. The residue obtained after filtration was again resuspended in equal volume of 95% ethanol for 48h and filtered again. The above two filtrates were mixed and solvent were evaporated in a rota vapour at 40-50.,a°C under reduced pressure. A dark semisolid material (9%) obtained was stored at 0- 40.,a°C until used.Hundred grams of dried and finally powdered Annona squamosa barks were suspended in 250 ml of water for 2h and then heated at 60-65.,a°C for 30 minutes. The extract was preserved and the process was repeated three times with the residual powder each time collecting the extract was pooled and passed through a fine cotton cloth. The above filtrate

upon evaporation at 40.,a°C yielded 16% semisolid extract.This was stored at 0-40.,a°C until used.

3.5 Curcuma Longa

Curcuma longa or turmeric is a tropical plant native to southern and southeastern tropical Asia. A perennial herb belonging to the ginger family, turmeric measures up to 1 m high with a short stem and tufted leaves. The parts used are the rhizomes. Perhaps the most active component in turmeric is curcumin, which may make up 2 to 5% of the total spice in turmeric. Curcumin is a diferuloylmethane present in extracts of the plant. Curcuminoids are responsible for the yellow color of turmeric and curry powder. They are derived from turmeric by ethanol extraction. The pure orange-yellow, crystalline powder is insoluble in water. The structure of curcumin (C21H20O6) was first described in 1815 by Vogel and Pellatier and in 1910 was shown to be diferuloylmethane by Lampe et al.[83] Chemical synthesis in 1913 confirmed its identity.[84] Turmeric is widely consumed in the countries of its origin for a variety of uses, including asa dietary spice, a dietary pigment, and an Indian folk medicine for the treatment of various illnesses.It is used in the textile and pharmaceutical industries[85] and in Hindu religious ceremonies in one form or another. Current traditional Indian medicine uses it for biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis.[86] The old Hindu texts have described it as an aromatic stimulant and carminative.[87] Powder of turmeric mixed with slaked lime is a household remedy for the treatment of sprains and swelling caused by injury, applied locally over the affected area. In some parts of India, the powder is taken orally for the treatment of sore throat. This nonnutritive phytochemical is pharmacologically safe, considering that it has been consumed as a dietary spice, at doses up to 100 mg/day, for centuries.[88] Curcumin is not water-soluble, but it is soluble in ethanol or in dimethylsulfoxide. Numerous reports

suggest that curcumin has chemopreventive and chemotherapeutic effects. Its anticancer potential in various systems was recently reviewed.[89] Curcumin blocks tumor initiation induced by benzo [a] pyrene and 7,12dimethylbenz [a] anthracene[90], and it suppresses phorbol ester-induced tumor promotion[91,92] In vivo, curcumin was found to suppress carcinogenesis of the skin[93-96], the forestomach[97,98], the colon[99-101], and the liver[102] in mice. Curcumin also suppresses mammary carcinogenesis[103–105] Compounds that block or suppress the proliferation of tumor cells have potential as anticancer agents. Curcumin has been shown to inhibit the proliferation of a wide variety of tumor cells, including B-cell and T-cell leukemia[106–109], colon carcinoma[110], and epidermoid carcinoma cells.[111] It has also been shown to suppress the proliferation of various breast carcinoma cell lines in culture.[112–114] We showed that the growth of the breast tumor cell lines BT20, SKBR3, MCF-7, T47D, and ZR75-1 is completely inhibited by curcumin, as indicated by MTT dye uptake,[3H] thymidine incorporation, and clonogenic assay.[112] We also showed that curcumin can overcome Adriamycin resistance in MCF-7 cells.[112] Recently, we have shown that curcumin can activate caspase-8, which leads to cleavage of Bid, thus resulting in sequential release of mitochondrial cytochrome C and activation of caspase-9 and caspase-3.[115] More recently, we have demonstrated that curcumin can suppress the proliferation of multiple myeloma cells.[115] Woo et al.[116] have demonstrated that curcumin can cause cell damage by inactivating the Akt-related cell survival pathway and release of cytochrome c, providing a new mechanism for curcumin-induced cytotoxicity. Zheng et al.[117] explored the apoptosis-inducing effects of curcumin in human ovarian tumor A2780 cells.

Alleviation of Side Effects several herbs have been described in ayurveda that can alleviate some of the common side effects associated with modern medical treatment of cancer. For instance, Bacopa monnieri has been shown to strengthen mental faculties and helps manage

insomnia or sleeplessness owing to stress. Similarly, an herbal combination based on the ancient rasayana formulations of Withania somnifera, Asparagus racemosa, Hydrocotyle asiatica, Nardostachys jatamamsi, Elettaria cardamomum, Tribulus terrestris, Zingiber officinalis, and Eclipta alba could also be useful in the treatment of anxiety, tension, and insomnia. Ocimum sanctum is beneficial against stress and depression during cancer. Yoga, meditation, prayer, and chanting can help release mental and physical stress.

Table: 1 List of cancer with list of drugs & the possible side effects

Types of cancer	List of drugs	Side effects
Lung cancer	Paclitaxel, Taxol, docetaxel, Tamoxifen, Vinorelbine, Gemcitabine, Topotecan, Irinotecan	Low white blood counts, low platelet count, anemia, hair loss, soreness of the mouth, difficulty swallowing, diarrhea, nerve damage, allergic reactions, fluid retention.
Colorectal cancer	5-Fluorouracil (5-FU), Capecitabine (Xeloda), Oxaliplatin (Eloxatin)	diarrhea (which can be severe), nausea and vomiting, lowered white blood cell count, loss of appetite, hair loss, and weakness. This medication may also increase your risk for blood clots in the legs and lungs, mouth sores, fatigue, abdominal pain, and numbness and tingling in the hands and feet.
Stomach cancer	Epirubicin, Methotrexate, Etoposide	hair loss, diarrhea, poor appetite and menstrual irregularities, fatigue, skin changes, nausea and red-colored urine , cough, dehydration, facial flushing, a fast or irregular heartbeat, and abnormal bleeding or bruising joint pain, difficulty breathing, black stools and bloody urine.
Cervical cancer	carboplatin ,cisplatin , paclitaxel ,fluorouracil,5-FU, cyclophosphamide, ifosfamide	hair loss, stomach upset, and fatigue , nausea and fatigue,
Head and neck cancer	isotretinoin	Tiredness , Sore mouth and small mouth ulcers , Hair loss , Feeling sick (nausea) and vomiting , Anaemia , Bruising or bleeding , Lowered resistance to infection
Ovarian cancer	Bevacizumab , Topotecan	Hypertension, lowered levels of white blood cells in the blood, Perforations on the bowels, hair loss and nausea.

Fig-1Plants with anticancer properties

CONCLUSION

The main objective of this study is to find out the result of comparison between the effectiveness of modern and herbal medicine in the treatment of cancer and to identify

whether herbal medicine or modern medicine has less side effect, to prove that herbs being major focus in modern medicine nowadays. Other than that to increase awareness among patient about herbal medicine as well as modern medicine and their side effects in the treatment of cancer. Overall, this review provides a glimpse of the herbal and modern approach to cause, awareness, diagnosis and treatment of cancer. This review also attempts to reveal how these approaches can be employed in today's world. The cause of the lower incidence, mortality, and morbidity could be lifestyle and diet related; the question of whether it is due to Ayurvedic principles leading to a better diet and lifestyle is difficult to pinpoint. Ayurvedic treatments are still followed by most of the world community for example 75 to 80% of the rural population of India use herbal medicine to treat basic ailments. As much as 70% of the Indian population is vegetarian, and this may also contribute to the lower incidence of cancer. This data shows that consumption of herbs or vegetarian food would reduce the chances of cancer, however, raises several questions about current treatment. Although current treatment tends to be highly focused at the molecular level, it is highly unfocused at the whole organism level, making it reductionist. Ayurvedic treatment of cancer is a holistic approach and is currently preferred. The new wave of ''system biology'' and ''genome revolution'' is expected to provide a holistic approach to the treatment of cancer. In spite of it, this approach tends to ignore the relationship between mind, body, and spirit. It is our hope that ayurveda can help fill this gap. Plant derived - botanical and dietary supplements which are widely prescribed world wide and are considered natural, safe and beneficial. Interest has revived recently in the investigation of medicinal plant to identify normal active phytochemicals that might lead to drug development as anticancer drugs derived from research on plant anti tumour agents.

Hence, we can conclude that there is more scope to explore herbal medicine into modern medicine as it is safer as well as economical. This review may help the students, researcher and health care professional to conduct further study which may be useful in finding of new anti cancer drugs.

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