Inti. Chern. Pharm. Med. J. Vol. 2(1), pp.153-161 (2005)

NEW SUCCESS IN THE CURE OF URINARY BLADDER CANCER WITH DRUGS OF NATURAL ORIGIN

Mansoor Ahmad I, **Syed Mahboob AIam2 and Muhammad Nadir2** *IResearch Institute of Pharmaceutical Sciences, Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan 2Dr. Nadir Research Institute of Cancer, Nadir Charitable Homoeopathic Hospital, Main Super Highway, Karachi, Pakistan*

ABSTRACT: Among the major problems of health, cancer is a challenge that scientists and medical doctors have to face. Thousands of scientists through out the world are trying to find out the exact cure of cancer. In spite of the presence of 402 medicines, the disease is spreading uncontrollably and the medicines that are available in the market are also not free from side effects and complications. Our group is searching for best solution. During the last 5 years great success was achieved in case of urinary bladder cancer.

Worldwide urinary bladder cancer is an important cause of morbidity and mortality especially in the old age group. In 2000, 260,000 new cases of the said disease came to light and 99,000 deaths occurred due to it. The occurrence rate in bladder tumor type is > 90% transitional cell carcinoma, 3-8% squamous cell carcinoma and I - 2% adenocarcinoma.

The extract of *Thuja occidentalis*, a well known ornamental plant, having anticancer potentials" was used as a major drug and *Taraxacum officinale* (another garden plant of medicinal value) extract as a supporting drug, in dilute dosage forms (10M, 10 10M, 101M 10200, 10100, 1030 and 106M). Both these drugs worked significantly (without any side effect and complication) and cured the disease within a short period. Treatment results (disappearance of painful symptoms) usually appeared in 1-3 months, reduction in tumor size in a year and non-recurrence of the disease in 2 years. 92% results were obtained in the treatment of 25 patients having bladder cancer of stage 3 or 4.

The possible mechanism action of these herbal drugs is also determined during this study. The method of treatment of cancer used here is actually opposite to conventional method. The secret of success of treatment is in dilute dosage and the use of drug of natural origin.

KEY WORDS: *Thuja occidentalis, Taraxacum officinale,* Carcinoma, Urinary Bladder Cancer, Adenocarcinoma.

INTRODUCTION

It is a well-known fact that 75% of cancer are due to environmental factors and some of them are with in the control of individuals like giving up of tobacco smoking, unnecessary fatty and heavy protein food, excessive exposure to sun, ultraviolet, infrared lights, magnetic, electromagnetic fields, use of nylon/poly-ethylene products, dairy products derived with steroids, pesticides etc. However, when cancer develops in a person neither he knows it nor does the doctor. The treatment usually starts on the basis of symptoms therefore clinically it is detected at 2nd, 3rd or 4th stage when the complications reach to the maXimum.

It is reported that one in three people in the developed countries is a cancer patient and one in four die from it. The rate of incidence is reported to be increasing from 10 to 20 million per year and rate of death is expected to increase from 6 to 10 million by 2020 (Strohman, 2001; WHO, 1998; Workman, 2001). The cure rate of certain cancer; like childhood cancer, testicular cancer, leukemia and lymphoma have been increasing despite the use of 92 FDA approved anticancer drugs.

However, the goal of cure, treatment and management is still frustrating and the development of anticancer drug is more challenging nowadays in spite of advancement in technology. In some cases surgery aml/radiation therapy is no longer to be curative/ effective or after surgery/radiation an improv~d systemic therapy is necessary for the treatment of patients with advanced metastatic cancer. Our group has the following:

- to provide relief to patients,
- to reduce treatment cost burden on patient,
- to find out drugs of natural origin having no side effects,

In this regard, a five years plan was chalked out and great successes were achieved. This paper deals the discovery, mode of action of drugs, and the treatment modalities of cancer.

Table 1. Reported chemical constituents of *T. occidentalis* & *T. officinale*

	Chemical Compounds
Thuja occidentalis	Oils; *a*-, f3-eudesmol, occidol, occidiol d-a-pinene, f3-pinene, d-a-thujone, f3-thujone, l-fenchone, l-borneal, borneol, terpeneol, sabinene, camphene, camphor, tannin, resin, mucilage, vitamin C, acids; acetic, formic, isovaleric, valerenic acid, sterol; 13-sistosterol, flavonoid; quercetine, and pigment; rhodoxanthine, etc.
Taraxacum officinale	Polysaccharides of fructosane and inulin type: inulin, levulin, helenin, glutin, gum, resin, pectin, vitamin; A, B, B2 (Riboflavin), C, E and K, protein, niacin, nutritive salts, elements; Ca, *Co*, Cu, Fe, Mg, Ni, P, CI, K, K salts, Si, Na, Sn, Zn, phytosterols; taraxacin, taraxacerin, taraxasterol, homotaraxa- sterol, taraxerol, sitosterin, stigmasterin, phytosterin, f3-amyrin, flavonoids; luteolin-7 -a-glucoside, luteolin-7 -O-diglucoside, hydroxyphenols; hydro-cinnamic acid, chicoric acid, monocaffeoyltartaric acid, chlorogenic acid, cichoriin, esculin, terpene; f3-carotene, non-provitamin A, pigments; xanthophyll, chlorophyll etc.

The Disease

Cancer is a group of many related diseases and it starts from abnormal growth of cells when they form a mass of tissue called a growth or tumor. Tumor may be benign or malignant. Benign tumors are not cancerous but malignant tumors are cancerous.

Malignant tumors are generally more dangerous than any other kind because the cancer cells have invaded and damaged nearby tissues and organs. Sometimes the cells break way from a malignant tumor and enter the blood stream or the lymphatic system. In this way the primary tumor forms a new tumor in other organs. The spread of cancer is known as metastasis (Kumar, 1992; Graham-Smith, 2002).

The Bladder Cancer

The wall of the bladder is lined with cells called transitional cells and squamous cells. More than 90% of bladder cancer starts from the transitional cells, therefore, it is known as transitional cell carcinoma. About 8% of bladder cancer patients have squamous cell carcinoma.

Cancer in the cells of lining of the bladder often comes back after treatment. Lining cell cancer often grows into the muscular wall of bladder and if it spreads to nearby organs then it causes cancer of uterus or vagina (in women) or prostate gland or abdominal wall or lymph nodes (Workman, 2001; Kumar, 1992; Graham-Smith, 2002).

The *most* common symptoms of bladder cancer are:

Blood in urine (Haematuria; making the urine slightly rusty *to* deep red)
Pain during urination, and
Frequent urination, or feeling the need *to* urinate without results.

These symptoms may appear in infections, benign tumor, bladder stones, or other problems may also cause these symptoms (McDermed, 2002).

The Drugs of Natural Origin

In the search of anticancer drugs we have screened out hundreds of drugs of natural origin (e.g. plants, animals, inorganic and organic acids, minerals etc.), but success was achieved in two herbal drugs i.e. *Thuja occidentalis* and *Taraxacum officinale.* Other supporting drugs used *to* prevent recurrence of symptoms are, *Lycopodium clavatum*, Sarsaparilla, *Atropa belladonna*, *Cantharis vesicatoria*, *Apis mellifica*, *Conium maculatum*, Nitric acid, Phosphorus, Sulphur, Terebinthina, Syphilinum, Medorrhinum, Tuberculinum,Sarsaparilla etc.

Thuja occidentalis L. (White Cedar; Cupressaceae)

It is a medium sized, monoecious, evergreen tree. It grows through out the world. It is cultivated in gardens as an ornamental plant. It has great value in the cure of tumors. Its chemical constituents are given

Table 2. Pharmacological and medicinal uses of *T. occidentalis* & *T. officinale*

	Uses
Thuja occidentalis	Mother tincture is used in folk remedies for benign skin cancer, tumors, condylomata (of penis and vulva), excrescence, fungus flesh, neoplasm, papilloma, plantar warts, polyps, tumors and warts. It is reported to be anaphrodisiac, diaphoretic, diuretic, lactagogue, and laxative, remedy for burns, colds, consumption, cough, debility, distemper, dysentery, dysmenorrhea, fever, gout, headache, inflammation, malaria, paralysis, rheumatism, swollen extremities, toothache and worms. The toxicity and fatalities are reported from the use of oil as abortifacient.
Taraxacum officinale	Abscesses, acne, age spots, anemia, appetite, antibiotic (weak), arteries (strengthens), artherosclerosis, biliousness, bladder, blisters (external), blood purifier, blood sugar, blood thinner, boils, breast cancer, breast abscesses, bronchitis, cancer prevention, cardiac oedema, cell metabolism, chicken pox fever, circulation, cirrhosis, cleaning gently: bladder, blood, kidneys, liver, whole body; colds, colitis, colon cleansing, congestive heart failure, connective tissue, constipation, corn, cramps, cysts, dental problems, dermatitis, detoxification, diabetes, digestive, digitalis replacement, dropsy, dyskinasia of bile duct, dyspepsia, eczema, endurance, energize, facial steams, fatigue, female reproductive organs, fever, flu, gall bladder, gall bladder obstructions, gall stone, gastro-intestinal problems, general debility, gout, headache, hemorrhoids, hepatitis, hepatogenic dropsy, high blood pressure, hormone regulator, hypertension, hypoglycemia, indigestion, internal injuries, jaundice, kidneys, kidney diseases, kidney inflammation, kidney stones, laxative, lethargic, liver congestion, enlargement, insufficiency, obstructions, stones, tonic, other liver problems, lymphoma, measles fever, menstruation problems, metabolism stimulant, migraine, mumps (fever), nonspecific heart distress, normalize heart rhythms, normalize blood sugar, nutrient, obesity, pancreas obstructions, pneumonia, psoriasis, rheumatism, skin diseases, spleen obstruction, swollen breast, swollen feet, ulcer, upper respiratory infections, urinary tract infections, warts, weight loss, yeast infection (Candida). Its diuretic action is similar to Furosemide (1asix@).

in table 1. The reported pharmacology and medicinal uses of plant are given in table 2 (Guenther, 1948-1952; Hartwell, 1967-1971; List & Horhammer, 1959-79; Radford, 1968; Duke, 1983; Steinbeck, 2002, Erichsen-Brown, 1973).

Taraxacum officinale (Dandelion; Compositae)

It is a wild plant growing commonly in garden lawns. It has tremendous value in medicine. Other than medicine it is used as salad greens, vegetable or fodder for animals. Its chemical constituents are given in table 1. Dandelion is used as whole, root leaves and blossom in medicine. Its different parts show excellent properties for different kind of diseases (Foster & Duke, 1990; Jones, 1994; Lust, 1974; Moore, 1990; Ottariano, 1999; Baba *et ai.,* 1981; Tiao-Zhong, 1996; Murray & Pizzorno, 1991; Stansbury, 1997; Kapoor, 1990; Cordatos, 1992; Williams *et ai.,* 1996; Hannemann, *et ai.,* 1985; Akhtar, *et ai.,* 1985; Vogel, 1977; Racz-Kotilla *et ai.,* 1974; Luo, 1993; Kim *et ai.* 1998; Chakurski *et ai.,* 1981); Lovell & Rowan, 1991; Hirono *et ai.,* 1978; Monograph, 2002) (Table 2).

The contraindications of *Taraxacum officinaie* are in diabetes mellitus, kidney and cardiac problems. In some people dandelion may cause allergy due to latex of sap from fresh plant material (Monograph, 2002).

The Treatment of Disease

In Dr. Nadir Research Institute of Cancer several hundred cases of different malignancies were treated during the last 20 years and great success has been achieved in each type of malignancy. The rate of cure and non-recurrence were recorded according to international standard. The maximum success (i.e. 92%) was recorded in the case of urinary bladder cancer. Therefore, in this paper we are presenting only the data and method of treatment. We adopted a slight different method of treatment from the usual way. After usual screening of the patient i.e. physical examination and test reports (Blood CP, Biochemistry, Lipid profile, LFT, Urine DR, Creatinin, BUN, Uric acid, Urea, special tests, ultrasound, Intravenous Pyelogram (X-ray), MRI, NMR, CT scan, Cystoscopy (biopsy) etc.), and on confirmation of malignancy/stage of disease, the treatment starts with a dose of anticancer drug that is *Thuja occidentalis* in dilute form. After a period of 4 days, on fifth day regular treatment starts with proper doses (in dilute form) of *Taraxacum officinale* for at least one month. Usually symptoms of cancer disappear in a month's time but if complaint remains there then repeat the same procedure. Next month symptoms disappear completely. If any other type of complaint like burning in urine, blood occasionally, oedema, are there then start symptomatic treatment with other supporting drugs like nitric acid, *Lycopodium clavatum,* Sarsaparilla, *Atropa belladonna, Cantharis vesicatoria, Apis mellifica, Conium maculatum,* Phosphorus, Sulphur, Terebinthina, Syphilinum, Medorrhinum etc. (All must be used in dilute form. Dilution method is given in dosage heading of this presentation.). During the first three months patients feel better, no blood in urine, painless urination, no oedema etc. but size of tumor remain the same. The reduction in size of tumor starts after 6 months therapy and disappears in a year. The treatment remains continued for one more year until all symptoms disappear and patients feel perfectly all right.

Dosage:

The usual drug dosages are in liquid and dilute forms. Globules of sugar of milk are used as vehicle for drug transportation to the site of action. The detail of drug dilution is given below:

Crude extract in alcohol (96%) diluted in I: 10 ratio in alcohol until the desired dilution is achieved i.e.

1050M 1010M 101M 10200 10100 1030 and 106 The extracts or prepared dosage are obtained either from Willmar Schwabe (Germany) or Boerick & Tafel (USA).

Patient Doses:

Thuja occidentalis: First dose 105OM, 101OM, 101M 10200, 10100, 1030 or 106 is given once only or is repeated if symptoms persist. The severity, complication, and stages of cancer determine dilution or potency. Usually low dilution is given in chronic cases and high in *l.ess* chronic cases. Single dose consists of 3 drops of potency in a cup of water or on 150 globules of sugar of milk.

Taraxacum officinale: First dose on fifth day of *Thuja occidentalis* in 1030 dilution 3 or 4 times a day till disease disappears. Single dose consists of 3 drops of potency in a cup of water or on 150 globules of sugar of milk.

Sometimes during recovery some other kind of symptoms appear like burning in urine, blood (occasionally), oedema, cough, dyspepsia, drowsiness, weakness, constipation, skin allergy, scanty and painful menses (in case of female), pain in kidney etc. **In** such cases symptomatic treatment is used.

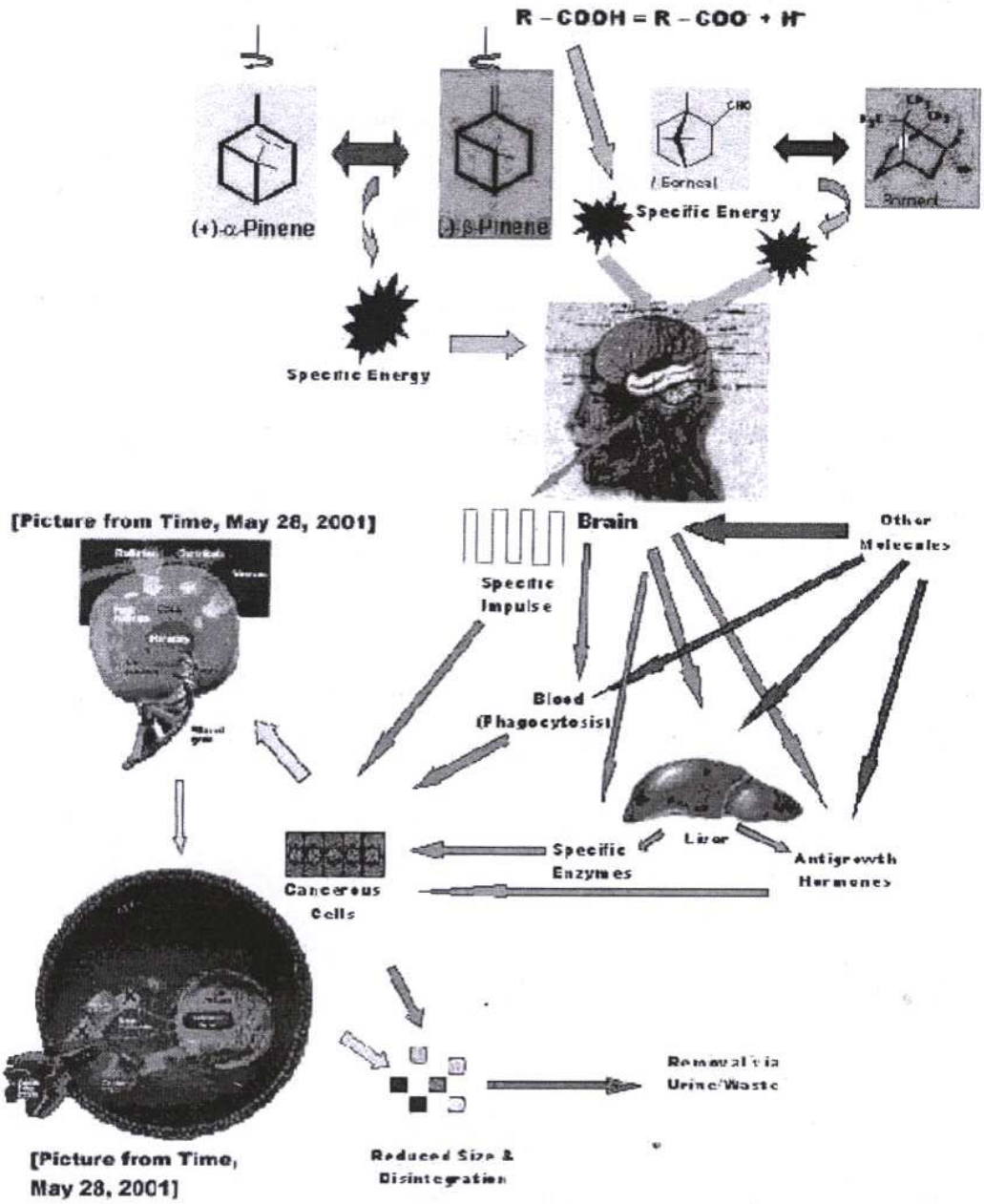
Treatment Results:

During a period of 5 years 50 patients of urinary bladder cancer were treated with the method described above with different drugs. But success was achieved with the combined effects of *Thuja occidentalis* and *Taraxacum officinale* in 25 patients. The rate of success was found 92 % (out of **25** patients **23** got off from urinary bladder cancer, **one** patient left the treatment and **one** died after six months) with out any complication or side effects. Each individual is spending his/her life like the disease has never been occurred to him.

DISCUSSION:

The environment, physique of an individual, socioeconomic problem, industrialization and less use of natural products leads to a common but major challenging disease--cancer. Recent development in

Fig.1. Schematic Representation of Mode of Action of Natural Drugs



technologies and discovery of gene therapy helped very much in understanding the disease, the cause and the therapy but still challenge is there (Lemonick & Park, 2001).

Our group has started work on this challenging aspect with the aim that the disease has come from nature therefore its cure will be there.

Drugs developed/discovered in the past are developed with the aim to stop and kill the cancer cells. At this moment more than 402 anticancer drugs are present in the market and the activity of many of these drugs is related to inhibition of nucleic acid synthesis, but mechanism of action of each drug differs completely. The existing drugs of natural origin, having anticancer activity, belong to a wide range of chemical classes for example flavonoids, alkaloids, steroids, terpenoids, saponins, tannins, coumarins etc. Some compounds of these classes are antimitotic in nature, like colchicine, podophyllotoxin, vincristine and maytansine. They act by binding to the protein tubulin in the mitotic spindle, preventing polymerization and assembly into microtubules. Another natural compound, Taxol, is a completely different type of antimitotic agent. It promotes the assembly of microtubules and stabilizes them against depolymerization. Podophyl- lotoxin is a tubulin binder but its semi-synthetic derivative etoposide and teniposide inhibit DNA synthesis and replication via the enzyme topoisomerase II. Camptothecin works through topoisomerase I system (Evan, 1996; Cassady & Douros, 1980).

Flavonoids are another class of natural compounds and are widely present in vegetables their anticancer activity action is different than others. They are known for their anti-inflammatory and anti-allergic effects, for antithrombitic and vasoprotective properties, for inhibition of tumor promotion and as protective for the gastric mucosa. These effects are attributed to the influence of flavonoids on arachidonic acid metabolism (Evan, 1996).

A large number of anticancer natural drugs act through their alkaline/acidic centers and this act can be explained on acid-base theory. It has been observed that the anti-tumor activity possessing compounds are usually having *fx*-, ~-unsaturated ester, lactone ring, epoxide, ether linkages, alcoholic, amine nature or thiols. Acronycine, Baccharin, Elephantopin, Bruceantin, Ellipticine, Bouvardin, Fagaronine, Indicine-N-oxide, Acer saponin P, Cucurbitacin E, Allamandin are natural drugs having anti-tumor activity and their activities are totally dependent on electrophilic and nucleophilic nature of the exiting groups (Evan, 1996; Cassady & Douros, 1980).

All above and other anti-tumor compounds are toxic in nature. They kill cancerous as well as normal healthy cells too. The selectivity action is usually dependent on the transportation of agent into the cell, chemical and sterlc nature of the specific molecule. Specific features of the active molecule could be involved in the formation of molecular complexes with growth-regulatory biological acromolecules.

Such results diverted our attention towards the use of drugs in low concentration. When this idea was used in the treatment of the disease a number of successes were achieved in a very short period. We focused our concentration on the use of crude extract in dilute form. The best result, 92% were obtained when we treated urinary bladder cancer with *Thuja occidentaZis* and supporting drug *Taraxacum officinaZe.* Literature search showed their anticancer activity along with tonic & immuno-stimulating properties (Guenther, 1948-1952; Hartwell, 1967-1971; List & Horhammer, 1959-79; Radford, 1968; Duke, 1983; Steinbeck, 2002, Erichsen-Brown, 1973; Jones, 1994; Lust, 1974; Moore, 1990; Ottariano, 1999; Baba *et aZ.,* 1981; Tiao-Zhong, 1996; Murray & Pizzorno, 1991; Stansbury, 1997; Kapoor, 1990; Cordatos, 1992; Williams *et aZ.,* 1996; Hannemann, *et aZ.,* 1985; Akhtar, *et at.,* 1985; Vogel, 1977; Racz-Kotilla *et aZ.,* 1974; Luo, 1993; Kim *et aZ.* 1998; Chakurski *et at.,* 1981); Lovell & Rowan, 1991; Hirono *et aZ.,* 1978; Monograph, 2002; Gohle, 1988 & 1990).

To determine the mode of action of crude extract is quite challenging but with the knowledge of physiology, biochemistry, chemistry, physics and genetic engineering/gene therapy, we postulated the possible mode of action/mechanism of action of the herbal drugs (see Fig. 1).

As we know that four basic amino acids are responsible for the production of DNA, RNA, genes, nucleic acid, proteins, polypeptide etc. Any kind of change in sequencing of these 4 amino acids or alteration in the metabolism of a cell is resulted in the abnormality or the development of cancer. Nevertheless, how can we control the abnormality in metabolism or the growth of cancerous cells? A good presentation of the development and the growth of cancerous cells have been published in *Time, May* 28, *2001* (Lemonick & Park, 2001).

In cancer disease especially when it is in 3rd or 4th stage the growth of cancerous cells take place within cell and in organ(s). For understanding the mechanism or mode of action of drug look into the growth and development process of an individual after fertilization of egg. Each step in cell division and organ growth requires enzymes, growth hormones, antigrowth hormones, signal transducers/inhibitors, growth factors (Epidermal growth factor, Platelet derived growth factor, Fibroblast growth factors, Transforming growth factors [c and l.J and many cytokinase) etc. The nucleus or brain controls the mechanism or action of growth. The growth and inhibition of growth occurs via signal transducers and signal inhibitors. In case of single cell growth signals are received by the nucleus but in organ cell it is received *from* the brain. In each case signals are received in the *form* of impulse of specific frequency.

Now think about the natural drug extract which consists of several types of compounds and these known and unknown compounds are of diverse nature. During biosynthesis, plants convert radiant energy into chemical energy. Plants and animals utilize this energy according to their needs. When the extract of natural origin is used as a source of drug the human body utilizes this energy according to its demand/nature & disease of the body.

When drug is taken orally, it is absorbed readily through mucous membrane of buccal cavity and reaches the brain via blood stream, where it acts, stimulates and creates an electronic impulse of specific frequency. This specific frequency impulse triggers the *specific receptor* (signal transducers and / or inhibitors) of the system and brings the changes (i.e. environmental changes in the metabolism of cancerous cells, without affecting the healthy neighbour cells because of the specificity of the impulse) in metabolism. The healthy neighbour cells work at different energy level and cancerous cells at different level.

As mentioned above extract/drug contains several chemical compounds, some of them are in unstable condition or ionic state. Therefore, a quick conversion in their states takes place such as U-Pinene to UPinene or vice versa or acidic state to ionic or ionic to acidic state (Fig. I). In each case, either energy is released or absorbed as a resultant of it an impulse is produced due to the difference in electro-negative and electro-positive states of molecule. In other words the hidden energy (Potential Energy) of chemical compounds is converted into active energy (Kinetic Energy). When this energy enters into the cell or site it activates the growth inhibitors (polypeptide *factor)* as a result of it growth in cancerous cell stops automatically (Fig. 1).

In other words it can be summarized as the electrostatic forces of the molecule and the surroundings are responsible *for* the production of specific energy (Fig. 1). And this specific quantum energy produces the specific impulse, which is detected by the brain and as a result of it sends the specific impulse via specific receptor *for* the change in state/environment of cancer cells. As soon as the impulse reaches there an electronic alteration takes place in the biosynthesis pathway of cancerous cells, and this is the first indication of the action of drug. Simultaneously some other molecules act directly on the brain to give order *for* the production of specific enzymes to denature the unwanted products of cancerous cells. Side by side they help in the production of healthy contents of the cells too.

Some other molecules reach the bloodstream and activate the blood contents *for* the production of templates *for* phagocytosis. In other words the immune system becomes active and starts working against unwanted material responsible *for* the disease. At the same time some other molecules (having hepatoprotective properties) reach the liver through blood stream and where they restore the metabolism properties of the liver. In this way healthy liver works in a better way and brings the active changes in the physiological functions i.e. production of healthy blood contents, bile, pancreatic juice etc. (Fig. 1).

Other compounds of the drug act through brain and activate the antigrowth hormones. These hormones immediately reach the site of action and start their function. The action of the drug is restricted to the production of antigrowth hormones (Fig. 1). As such the drug has no direct action on the growth of cancerous cells. Therefore, no killing action has been found on healthy neighbour cells by the drug molecules.

One might ponder or imagine if the medicine could contain the drug in such dilutions like 105OM, 1OIOM,

101M 10200, 10100, 1030 or 106. Yes, a chemist can explain it very easily on the basis of Avogadro's theory, where Ig atomic mass or molecules contains 6.02 x 1023 particles and for alteration of any chemical reaction a single hydrogen ion is enough. Therefore, each system works at a specific energy level and any change results in abnormality and reverse order reaction restores the system.

Conclusion:

The drugs of natural origin are the safest drugs if they are used in dilute form. We have treated other types of cancer for example breast, brain, colon, leukemia etc. and found the same mechanism of action as described in fig. 1 but their results are slightly lesser than urinary bladder cancer. The work of finding the other fast action drug in dilute form like *Thuja occidenta/is* and *Taraxacum officinale* is under progress.

Acknowledgement:

The authors are deeply indebted to Dr. Syeda Humaira Nizami, Dr. Saima Jabeen, Dr. Irfana Shaheen, Dr. S. Manzoor Hussain, Dr. Farid Ahmad of Dr. Nadir Research Institute of Cancer for their assistance in case handling and data compilation. They are also thankful to Mr. Zeeshan Anwer Ali of NED University for computer assistance. The authors have an equal contribution in this research work. This work is also a part of the Ph.D. thesis.

References:

Akhtar, M.S., Khan, Q.M., Khaliq, T. Effects of *Portulaca oleracae* (Kulfa) and *Taraxacum officinale* (Dhudhal) in normoglycaemic and alloxan-treated hyperglycaemic rabbits. *J. Pak. Med. Assoc.*, 35, 207-210 (1985).

Saba, K. *et al.* Antitumor activity of hot water extract of dandelion, *Taraxacum officinale?* correlation between antitumor activity and timing of administration. *Yagugaku Zasshi*, 101, 583-43 (1981). [Article in Japanese]

Cassady, J.M., Douros, J.D. (1980). *Anticancer Agents Based on Natural Product Model.* Academic Press, New York.

Chakurski, I., Matev, M. Koichev, A. *et al.* Treatment of chronic colitis with an herbal combination of *Taraxacum officinale, Hypericum perforatum, Melissa officinalis, Calendula officinalis and Foeniculum vulgare. Vutr Boles*, 20, 51-54 (1981). [Article in Bulgarian]

Cordatos, E. (1992). *Taraxacum officinale.* In: Murray, M. & Pizzomo, J., eds. A Textbook of Natural Medicine. Bastyr University Press, Seattle.

Duke lA. *Handbook of Energy Crops.* (1983) (unpublished).

Erichsen-Brown, C. (1979). Use of plants for the past 500 years. Breezy Creeks Press, Aurora (Canada).

Evan, W.c. (1996). *Trease* & *Evans' Pharmacognosy.* W.B. Saunders Co. Ltd.

Foster, S. & Duke, J.A. (1990). A *field Guide to Medicinal Plants: Eastern and Central North America.* Houghton Mifflin Co., Boston, MA.

Gohle, S. (1988). *In Vivo-* und *in Vitro-untersuchungen* zur Immunmodulation des spezifischen Immunsystems durch Hochmolekulare Polysaccharidfraktionen der Cupressa-ceae *"Thuja occidentalis* L.". Dissertation. Hamburg.

Gohle, S. *et al.* (1990). *Immun- modulation am Biespiel der Cupressaceae 'Thuja occidentalis L.'* In: Albrecht, H., Franz, G. (eds.) Naturheilverfahren: Zum Stand der Forschung. Springer; Berlin, Heidelberg, New York. pp. 59-86.

Graham-Smith, D.G. and Aronson, J.K. (2002). *Clinical Pharmacology and Drug Therapy* (3ed Ed.). Oxford University Press Inc. New York. pp. 437 - 445.

Guenther, E. (1948 - 1952). *The Essential Oils.* 1-6 vols. D'van Nostrand Company Inc. New York.

Hannemann, K., *et al.* The common occurrence of furan fatty acids in plants. *Lipids* 24, 296-298 (1985).

Hartwell, J. L. Plants used against cancer. A survey. *Lloydia* 30-34, (1967 -71).

Hirono, I. *et al.* Safety Examination of Some Edible Plants Part 2. *J. Environ Pathol Toxicol.*, **1,71-74** (1978).

Jones, F. (1994). *Medicinal Herb Handbook.* Six Directions Publishing Cooperative, Boulder, CO.

Kapoor, L.D. (1990).The CRC Handbook of Ayurvedic Medicinal Plants. CRC Press, Boca Raton. p. 316.

Kim, H.M. *et al. Taraxacum officinale* restores inhibition of nitric oxide production by cadmium in mouse peritoneal macrophages. *Immuno-pharmacol. Immunotoxicol.*, 20, 283-297 (1998).

Kumar, V., Cotran, R.S., Robbins, S.L. (1992). *Basic Pathology* (5th Ed.). W.B. Saunders Company, London. pp. 467- 471.

Lemonick, M.D. & Park, A. *New Hope for Cancer. Time,* 42-49, May 28 (2001).

List, P.H. & Horhammer, L. (1969 - 79). *Hager's Handbuch der Pharmazeutischen Praxis.* 2-6 vols. Springer- Verlag, Berlin.

Lovell, C.R., Rowan, M. Dandelion Dermititis. *Contact Dermititis,* 25,185-188 (1991).

Luo, Z.H. The use of Chinese traditional medicines to improve impaired immune functions in scald mice. *Chung Hua Cheng Hsing Shao Shang Wai Ko Tsa Chih,* 9,56-58 (1993). [Article in Chinese]

Lust, J. (1974). *The Herb Book.* Bantam Books, New York.

McDermed, 1. (2002). *Laboratory Testing for Bladder Cancer Management.* Technical documents News & Views. Winter/Spring.

Monograph (2002): *Taraxacum officinale.* http://www.thorne.com/al tmedrev /dandalion4- 2.html

Moore, M. (1990). *Los Remedios: Traditional Herbal Remedies of Southwest.* Red Crane Books, Santa Fe, NM.

Murray, M. & Pizzorno, J. (1991). *Encyclopedia of Natural Medicine.* Prima, Rocklin, CA.. p. 301.

Ottariano, S.G. (1999). *Medicinal Herb Theraapy: A Pharmacist's View Point.* Nicolin Fields Publishing Inc., Portsmouth, NH.

Racz-Kotilla, E. Racz, G., Solomon, A. The action of *Taraxacum officinale* extracts on the body weight and diuresis of laboratory animals. *Planta Medica,* 26, 212217 (1974).

Radford, A.E., Ahles, H.E. and Bell, c.R. (1968). *Manual of the vascular flora of the Carolinas.* UNC Press, Chapel Hill.

Stansbury, 1. (1997). *Botanical Therapies for Fibrocystic Breast Disease.* Medical Herbalism, Summer. p. 1.

Steinbeck, M. (2002). *Arznei des Monats: Thuja occidentalis.* http://www.bunkahle.comlhomoeopathi e/ma tmed/thuj.htm

Strohman, R.C. Genomics and human Life Span - What's Left to Extend? *Nature Biotech,* 19,195 (2001).

Tiao-Zhong, Y. Herba Taraxaci Monolici Cum Radice (Pu Gong Ying) as the Main Treatment in Gynecological Recalcitrant, Difficult Conditions. Xi *Zhong Yi (New Chineese Medicine),* 5, 46 (1996).

Vogel G. (1977). *Natural substances with effects on the liver.* In: Wagner, H. (eds.) *New Natural Products and Plant Drugs with Pharmacological, Bio.logical or Therapeutic Activity.* Springer-Verlag, Heidelberg.

Williams, C.A., Goldstone, F., Greenham, J. Flavonoids, cinnamic acids and coumarins from the different tissues and medicinal preparations of *Taraxacum officinale. Phytochemistry* 42, 121-127 (1996).

Workman, P. New Drug Targets for Genomic Cancer Therapy: Successes, Limitations, Opportunities and Future Challenges. *Current Cancer Drug Targets,* **1(1),** 33-47 (2001).

World Health Report. Life in the 21 st Century. A Vision for All. *World Health Organization,* 1998.

Manuscript received 15-12-2003
Accepted for publication 16-12-2004