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(71) Demandeur/Applicant:
BIONOVO, INC., US

(72) Inventeur/Inventor:
COHEN, ISAAC, US

(74) Agent: FETHERSTONHAUGH & CO.

(54) Titre : EXTRAIT DE SCUTTELARIA BARBATA DESTINE A TRAITER LE CANCER
(54) Title: SCUTELLARIA BARBATA EXTRACT FOR THE TREATMENT OF CANCER

(57) Abrégé/Abstract:
An extract of Scutellaria barbata D. Don is effective in the arrest of cancer cell growth in the Gl phase, the induction of apoptosis in cancer cells and the shrinking of solid cancers. The extract may be prepared as a pharmaceutical composition for administration to mammals for the treatment of solid cancers, such as epithelial cancers. Such epithelial cancers include breast cancer and ovarian cancers. The extract is obtained from Scutellaria barbata D. Don by contacting aerial portions of a plant from the species Scutellaria barbata D. Don with an aqueous or alcoholic solvent.

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(71) Applicant *(for all designated States except US)*: **BIONOVO, INC.** [US/US]; 5858 HORTON STREET, SUITE 375, Emeryville, CA 94608 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **COHEN, Isaac** [US/US]; 5858 HORTON STREET, Emeryville, CA 94608 (US).

(74) Agents: **GRUMBLING, Matthew, V.** et al.; WILSON SONSINI GOODRICH & ROSATI, 650 PAGE MILL ROAD, Palo Alto, CA 94304-1050 (US).

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(54) Title: SCUTELLARIA BARBATA EXTRACT FOR THE TREATMENT OF CANCER

(57) Abstract: An extract of *Scutellaria barbata* D. Don is effective in the arrest of cancer cell growth in the Gl phase, the induction of apoptosis in cancer cells and the shrinking of solid cancers. The extract may be prepared as a pharmaceutical composition for administration to mammals for the treatment of solid cancers, such as epithelial cancers. Such epithelial cancers include breast cancer and ovarian cancers. The extract is obtained from *Scutellaria barbata* D. Don by contacting aerial portions of a plant from the species *Scutellaria barbata* D. Don with an aqueous or alcoholic solvent.

SCUTELLARIA BARBATA EXTRACT FOR THE TREATMENT OF CANCER

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from provisional United States patent application 60/736,620, filed on November 14, 2005, and United States patent application 11/559,324 filed November 13, 2006, both of which are incorporated herein in their entirety.

BACKGROUND OF THE INVENTION

[0002] While advances in early detection and adjuvant therapy for breast cancer have had a favorable impact on patient survival in general, patients who develop advanced metastatic breast cancer are generally likely to face a less favorable prognosis. Commonly used hormonal and chemotherapeutic agents can lead to transient regression of tumors and can also palliate symptoms related to cancer. However, these treatments are often accompanied by toxicities and intolerable side effects and eventually become ineffective in controlling advanced stage breast cancer and its symptoms. Improvements in survival are modest, even with newer targeted biological agents. Moreover, in most metastatic cancers resistance to available conventional treatment ultimately develops or excessive side effects are seen with conventional therapies.

[0003] It is interesting to note that greater than 60% of all chemotherapeutic agents used in the treatment of breast cancer are derived from natural substances (Newman 2003). A fairly recent example is the development of taxanes from the Pacific yew tree, *Taxus brevifolia*. Throughout the world, it is estimated that approximately 80% of the world population still relies on botanical medicine as the primary source of therapy. In the West, botanical medicine is considered a popular form of complementary and alternative medicine among patients diagnosed with cancer. However, few clinical trials have been conducted to firmly assess the safety and efficacy of botanical agents for the treatment of breast cancer, despite anecdotal case reports of cures and clinical efficacy in women who have relied solely on botanical medicine for treatment. It has previously been shown that the aqueous extract of *Scutellaria Barbata* can lead to growth inhibition of breast cancer cell lines in vitro ("Antiproliferative activity of Chinese medicinal herbs on breast cancer cells in vitro," Anticancer Res., 22(6C):3843-52 (2002)). BZL101, a concentrated aqueous extract of *Scutellaria Barbata*, was evaluated for antiproliferative activity on five breast cancer cell lines (SK-BR-3, MCF7, MDA-MB-231, BT-474, and MCNeuA). These cell lines represent important prognostic phenotypes of breast cancer expressing a range of estrogen and HER2 receptors. BZL101, tested at a 1:10 dilution (15μg/ ml), demonstrated >50% growth inhibition on four of the five cell lines (Campbell, 2002). BZL101 showed >50% growth inhibition on a panel of lung, prostate and pancreatic cancer cell lines. BZL101 at the same dose did not cause >25% of growth inhibition on normal human mammary cells (HuMEC), demonstrating selectivity to cancer cells (Table 1). More so, BZL101 had a mild mitogenic effect on normal human lymphocytes. In cell cycle analysis,

BZL101 caused an S phase burst and G1 arrest. BZL101 also attenuated mitochondrial membrane potential causing caspase-independent high molecular grade (HMG) apoptosis.

[0004] There is a need for therapies for treatment of patients having metastatic cancers. There is also a need for therapies with reduced, and more specifically minimal, toxicity for patients having metastatic cancers. In particular, there is a need for novel therapies with relatively low toxicity for the treatment of metastatic solid tumors, such as epithelial tumors, and more particularly breast and ovarian cancers.

[0005] These and other needs are met by embodiments of the invention.

SUMMARY OF THE INVENTION

[0006] The foregoing and further needs are met by embodiments of the invention, which provide a pharmaceutical composition for the treatment of cancer. The pharmaceutical composition according to the invention comprises a therapeutically effective amount of an extract of the herb *Scutellaria Barbata* D. Don. The pharmaceutical composition can also contain one or more optional excipients.

[0007] These and other needs are further met by embodiments of the invention, which provide a method of treating a patient suffering from cancer. The method comprises administering to a patient suffering from cancer a therapeutically effective amount of an extract of the herb *Scutellaria Barbata* D. Don.

[0008] Other uses and advantages of the present invention will be apparent to the person skilled in the art after having considered the description, including the drawings and claims, herein.

INCORPORATION BY REFERENCE

[0009] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0011] FIG. 1 shows dose-response curves showing the response of several solid cancer tumor cells to aqueous extract of the herb of this invention.

[0012] FIG. 2 shows dose-response curves showing the response of several breast solid cancer tumor cells to aqueous extract of the herb of the invention.

[0013] FIG. 3 shows dose-response curves comparing the response of breast solid cancer tumor cells and normal breast epithelium to aqueous extract of the herb of this invention.

[0014] FIG. 4 shows gel electrophoresis plate, which demonstrates that nuclear DNA disintegration occurs during apoptosis of solid tumor cancer cells in contact with aqueous extracts of the herb of this invention.

[0015] FIG. 5 shows the effect of the herb extract of the invention administered intraperitoneally (IP) on the tumors of mice in a xenograft model.

[0016] FIG. 6 shows the effect of the herb extract administered by oral gavages and in interaction with cyclophosphamide administered in low dose in the drinking water on the tumors of mice in a xenograft model.

[0017] FIG. 7 shows that the herb extract induces apoptosis without activating caspases.

[0018] FIG. 8 shows that the herb extract in cell cycle analysis arrests the cells at the G1 phase.

DETAILED DESCRIPTION OF THE INVENTION

[0019] This invention relates to extract of *Scutellaria barbata* where the extract, when placed in contact with solid tumor cancer cells, inhibits the activity, that is the growth and/or proliferation, of the cells. The herb is selected from the species *Scutellaria barbata* D. Don of the Labiatae Family. **Herba *Scutellaria* Barbata D. Don** (Lamiaceae) of the Labiatae family- Ban Zhi Lian (BZL) is grown mainly in areas southeastern of the Yellow River (Huang Po) in the provinces of Sichuan, Jiangsu, Jiangxi, Fujian, Guangdong, Guangxi and Shaanxi but not exclusively. The plant is harvested in late summer and early autumn after it blooms (May-June). The aerial part is cut from the root. Only the aerial part (leaves and stems) is used for BZL101. The herb is dried in the sun and packed as a whole plant. The herb is received with no separation between leaves and stems.

[0020] As is described in the Detailed Description section, below, the herb is substantially more active in inhibiting the activity of different types of cancer cells. It is therefore a presently preferred aspect of this invention that the herbal extract obtained from the species *Scutellaria barbata*. It is a particularly presently preferred aspect of this invention that the herbal extract is obtained from *Scutellaria barbata* D. Don.

[0021] It is an aspect of this invention that the solid tumor cancer cell, the activity of which is inhibited by the herbal extract of this invention is a SKBR3 cell, a MCF7 cell, a MDA-MB231 cell, a BT474 cell or a MCNeuA cell (breast cancer cells), A549 cell, LLC cell (Lung Cancer cells), Panc1 cells, Panc02 cells (Pancreatic cancer cells), PC-3 cells LNCaP cells (Prostate Cancer cells), OVCAR cells, SKOV3 cells (Ovarian Cancer cells). In some embodiments of the invention, the cell line is *in vivo*, i.e. a xenograft of the tumor line is present in a mammalian model animal, such as a mouse, rat, dog, cat, sheep, goat or other mammal. Thus, the extract of *Scutellaria barbata* can be used as a standard for the evaluation of potential anti-cancer drugs.

[0022] A further aspect of this invention is a method for treating a solid tumor cancer, comprising administering to a patient a therapeutically effective amount of a composition comprising an extract of *Scutellaria barbata*. It is a presently preferred aspect of this invention that the pharmaceutical composition used to treat a patient comprises an extract of *Scutellaria barbata*. It is further a particularly presently preferred aspect of this invention that the extract used to treat a patient is obtained from the herb species *Scutellaria barbata* D. Don.

[0023] The solid tumor cancer being treated is an epithelial cell cancer in another aspect of this invention.

[0024] The epithelial cell cancer is breast or ovarian cancer in a still aspect of this invention.

[0025] An aspect of this invention is a composition comprising a pharmaceutically acceptable carrier of excipient and an extract *Scutellaria barbata.*

[0026] The pharmaceutical composition comprises aqueous extracts of the above herb species in an aspect of this invention.

[0027] The pharmaceutical composition comprises alcohol extracts of the above species in a further aspect of this invention. In a presently preferred embodiment of this invention, the alcohol used to extract the herbs is ethyl alcohol.

[0028] The pharmaceutical composition comprises a combination of aqueous and alcohol extracts of the above species of herb in still another aspect of this invention.

[0029] **Table 1** depicts the herb, from which extracts of this invention are obtained, listed by family, genus, species and tradition Chinese name, of this invention

Table 1

Family	genus	Species	Chinese name	Herb part
Labiatae	Scutellaria	Barbata D. Don	Ban Zhi Lian	aerial

[0030] **Table 2A** shows the degree of inhibition of the activity of several *in vitro* solid breast cancer tumor cell lines by the extract of this invention.

Table 2A

MCF7	SKBR3	MDA-MB231	BT474	MCNeuA
++	++	++	+	++

[0031] **Table 2B** shows the degree of inhibition of the activity of several *in vitro* solid cancer tumor cell lines by the extract of this invention.

Table 2B

Lung Cancer		Pancreatic Cancer		Prostate Cancer		Breast Cancer		Breast Normal
A549	LLC	Panc1	Panc02	PC-3	LNCaP	MCF7	MCNeuA	HuMEC
+	++	+	++	+	+	++	++	-
1424	492	1054	594	1035	1516	818	619	

- < 50% inhibition, + 51-75% inhibition, ++ >75% inhibition, IC_{50} values (μg/ml)

[0032] The active ingredients in BZL101 are not known. The extract loses activity when reconstituted after drying, as well as when the extract is separated through physical and chemical means. The known chemical ingredients in the plant are scutellarin, scutelarein, carthamidin, isocarthamidin and wagonin.

Definitions

[0033] As used herein, the term "method" refers to manners, means techniques and procedures for accomplishing a given task including, but not limited to, those manners, means techniques and procedures either known to, or readily developed from known manners, means, techniques and procedures by, practitioners of the chemical, pharmacological, biological, biochemical, medical, and homeopathic arts.

[0034] As used herein, "inhibiting the activity" refers to slowing, preferably stopping, the growth and/or proliferation of cancerous cells, both in-place, i.e., growth and proliferation at the initial site of tumor formation, and proliferation by metastasis. Inhibiting the activity also encompasses, in fact it is the most preferred embodiment of this invention, killing cancerous cells.

[0035] As used herein, the term "cancer" refers to various types of malignant neoplasms, most of which can invade surrounding tissues, and may metastasize to different sites, as defined by Stedman's Medical Dictionary 25th edition (Hensyl ed. 1990). Examples of cancers which may be treated by the present invention include, but are not limited to, brain, ovarian, colon, prostate, kidney, bladder, breast, lung, oral and skin cancers. In a presently preferred embodiment of this invention the cancer being treated is breast or ovarian cancer.

[0036] As used herein, the term "contacting" in the context of contacting a solid tumor cancer cell with an extract of this invention bringing an extract of this invention and a target cancer cell together in such a manner that the extract can affect the activity of the cell either directly or indirectly. As used herein, contacting refers to procedures conducted *in vitro*, i.e. cancerous cells which are the object of this invention are studied, outside a patient. Cells existing outside the patient can be maintained or grown in cell culture dishes. For cells outside the organism, multiple methods exist, and are well-known to those skilled in the art, to contact extract of this invention, with or without employment of various well-known transmembrane carrier techniques and direct cell microinjection

[0037] The term "*in vivo*" refers to contacting or treatment within a living organism, such as a living human or other mammal, such as a mouse or rat.

[0038] As used herein, an "extract" refers to the residue of soluble solids obtained after an herb, or selected part thereof is (1) for example, without limitation, chopped, crushed, pulverized, minced or otherwise treated to expose maximum surface area and (2) is placed in intimate contact with a liquid, usually, but not necessarily, under conditions of agitation and elevated temperature. Then, after a period of time under the foregoing conditions the mixture is filtered to remove solids and the liquid is removed by, for example but not limitation, evaporation or freeze drying. The liquid used to obtain an extract may be water or an organic solvent, for example, without limitation, an alcohol such as methyl, ethyl or isopropyl alcohol, a ketone such as acetone or methyl ethyl ketone (MEK), an ester such as ethyl acetate, an organochlorine compound such as methylene chloride, chloroform or carbon tetrachloride, a hydrocarbon such as pentane, hexane or benzene and the like. An extract may also be obtained by using a combination of these solvents with or without water.

[0039] As used herein, an "herb" refers to any plant that is reputed to have medicinal value in Traditional Chinese Medicine (TCM). That is, the use of extracts of various parts of these plants have been passed down from ancient to modern Chinese practitioners of herbal medicine as a means for treating various ailments. In some instances, clinical evidence using standard Western medical research protocols have verified the utility of some of the extracts. While each of the herbs, and parts thereof, that make up The pharmaceutical compositions of this invention have long been known in TCM, use of an extract or combination of extracts in a composition as disclosed herein for the treatment of solid tumor cancers, in particular breast and uterine cancer, has not been previously disclosed. In particular embodiments of the invention, the herb is *Scutellaria barbata*, especially *Scutellaria barbata* D. Don.

[0040] As used herein, the terms "treat", "treating" and "treatment" refer to a method of alleviating or abrogating a solid tumor cancer and/or its attendant symptoms. In particular, the terms simply mean that the life expectancy of an individual affected with a cancer will be increased or that one or more symptoms of the disease will be reduced.

[0041] As used herein, "administer", "administering" or "administration" refers to the delivery of an extract or extracts of this invention or of a pharmaceutical composition containing an extract or extracts of this invention to a patient in a manner suitable for the treatment of particular cancer being addressed.

[0042] As used herein, the term "mammal" refers to any mammal that is affected by a cancer, whether that cancer is autologous (*i.e.* arises naturally in the mammal) or is of xenogenous (*i.e.* xenogenic) origin. The term "mammal" includes humans, as well as murine, canine, feline, equine, bovine, ovine, porcine and other mammalian species.

[0043] A "patient" refers to any higher organism that is susceptible to solid tumor cancers. Examples of such higher organisms include, without limitation, mice, rats, rabbits, dogs, cats, horses, cows, pigs, sheep, fish and reptiles. In particular examples, "patient" refers to a human being.

[0044] As used herein, the term "therapeutically effective amount" refers to that amount of an extract or combination of extracts of this invention which has the effect of (1) reducing the size of the tumor; (2) inhibiting (that is, slowing to some extent, preferably stopping) tumor metastasis; (3) inhibiting to some extent (that is slowing to some extent, preferably stopping) tumor growth; and/or, (4) relieving to some extent (or preferably eliminating) one or more symptoms associated with cancer (5) stabilizing the growth of the tumor, (6) extending the time to disease progression, (7) improving overall survival.

[0045] As used herein, a "pharmaceutical composition" refers to a mixture of one or more of the extracts described herein with other chemical components, such as physiologically acceptable carriers and excipients. The purpose of a pharmacological composition is to facilitate administration of an extract or extracts of this invention to patient.

[0046] As used herein, the term "pharmaceutically acceptable" means that the modified agent or excipient is generally regarded as acceptable for use in a pharmaceutical composition.

[0047] As used herein, a "physiologically acceptable carrier" refers to a carrier or diluent that does not cause significant irritation to an organism and does not abrogate the biological activity and properties of the administered composition.

[0048] As used herein, an "excipient" refers to an inert substance added to a pharmaceutical composition to further facilitate administration of an extract or extracts of this invention. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils and polyethylene glycols.

[0049] At one time, botanical agents were the most significant group of substances used by healers to treat patients. According to a WHO survey, 80% of the world's population still relies heavily on herbal medicine as their primary source of therapy. In Western culture one-quarter of the active components of currently prescribed drugs were first identified in plants and over half of the 50 most popular drugs today are derived from plant materials. In addition, over 60% of chemotherapeutic agents used in the treatment of cancer are derived from natural substances.

[0050] A useful strategy for the discovery of biologically active compounds from plants is the ethno-pharmacological approach which uses information about traditional medicinal uses of plants. The long history of a plant's use in treating a disorder, regardless of whether the disorder is well-characterized, e.g., skin rash, or is rather more nebulous, e.g., hot blood, is a clear indicator that something in the plant has some manner of beneficial effect on a disorder, otherwise the use of the plant would have faded in time. Furthermore, the fact that homeopathic practitioners have been administering the plant or an extract thereof to human patients for, often, centuries provides a compelling argument for the safety of the plant or its extracts in human beings.

[0051] Such alternative approaches to medicine are becoming more and more widely accepted and used in the United States as well to treat a broad spectrum of conditions as well as to maintain wellness. It is estimated that one in two Americans currently uses alternative therapies at one time or another. In particular, the most popular complementary or fully alternative approach to the treatment of their cancers by patients is botanical agents/herbal medicines.

[0052] Traditional Chinese medicine (TCM) is often the treatment modality of choice by cancer patients opting for an alternative approach to dealing with their ailment. Patients use TCM both as anti-cancer agents and to alleviate the side effects of standard chemotherapy. However, TCM lacks the scientifically sound methodology required of Western pharmacology and the use of TCM is often hit or miss in its effectiveness. There remains a need for the discovery of specific herbal extracts and combinations thereof that have a specific utility and for which there is scientific evidence as to why they work in that use. This invention provides such extract and compositions decoction.

Pharmaceutical Compositions and Modes of Administrations

[0053] An extract of this invention can be administered to a patient either as a "tea," without combination with any other substances or further manipulation, or it can be administered as a pharmaceutical composition where the extract is mixed with suitable carriers or recipient(s). In treating a

patient exhibiting a disorder of interest, a therapeutically effective amount of the extract is administered. A therapeutically effective amount refers to that amount of the extract that results in amelioration of symptoms or a prolongation of survival in a patient, and may include destruction of a malignant tumor of a microbial infection.

[0054] When administered without combination with any other substances, the composition comprising extract of *Scutellaria Barbata* (especially *Scutellaria Barbata* D. Don) may be encased in a suitable capsule, such as a gelatin capsule. When administered in admixture with other excipients, adjuvants, binders, diluents, disintegrants, etc., the dry extract of *Scutellaria Barbata* may be compressed into a capsule or caplet in a conventional manner that is well-known in the art.

[0055] Toxicity and therapeutic efficacy of the extracts, i.e., determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population) can be determined by standard pharmaceutical procedures in cell cultures or experimental animals. The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Extracts that exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosages for use in humans, in particular for internal use, that include ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. In general, since the extracts used in the methods of this invention have been used in TCM, they are known to be relatively non-toxic to humans and therefore it is expected that they will exhibit large therapeutic indices.

[0056] For any extract used in the method of invention, the therapeutically effective dose can be estimated initially from cell culture assays. For example, a dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by HPLC.

[0057] The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition and based on knowledge of TCM. (*See e.g.* Fingl *et al.*, in THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 1975, Ch. 1, p. 1). It should be noted that the attending physician would know how and when to terminate, interrupt, or adjust administration due to toxicity, or organ dysfunction. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response is not adequate. The severity of the condition may, for example, be evaluated, in part, by standard prognostic evaluation methods. Further, the dose and perhaps dose frequency will also vary according to the age, body weight, and response of the individual patient. A program comparable to that discussed above may be used in veterinary medicine.

[0058] If desired, standard western medicine techniques for formulation and administration may be used, such as those found in Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Co., Easton, PA (1990). Suitable routes may include: oral, rectal, transdermal, vaginal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections; as

well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections, to name a just a few. In particular embodiments, the extract of the invention is administered orally.

[0059] For injection, an extract of this invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For such transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

[0060] Use of pharmaceutically acceptable carriers to formulate an extract herein use in the methods disclosed for the practice of this invention in dosages suitable for systemic administration is within the scope of the invention. With proper choice of carrier and suitable manufacturing practice, an extract of the present invention, in particular those formulated as solutions, may be administered parenterally, such as by intravenous injection. Likewise, an extract can be formulated, using pharmaceutically acceptable carriers well known in the art, into dosages suitable for oral administration. Such carriers enable extracts to be formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

[0061] Pharmaceutical compositions suitable for use in the present invention are compositions wherein an extract is contained in an effective amount to achieve its intended purpose. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. A pharmaceutical composition may contain suitable pharmaceutically acceptable carriers including excipients and auxiliaries that facilitate processing of the extracts into preparations that can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, dragees, capsules, or solutions. The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, e.g., by means of convention mixing, dissolving, granulating, dragees, capsules, or solutions. The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levitating, emulsifying, encapsulating, entrapping or lyophilizing processes.

[0062] Pharmaceutically formulations for parenteral administration include aqueous solutions of an extract in water-soluble form. Additionally, suspensions of an extract may be prepared as appropriate oily injection suspensions may contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents that increase the solubility of an extract to allow for the preparation of highly concentrated solutions.

[0063] Pharmaceutical preparations for oral use can be obtained by combining an extract with solid excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for

example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

[0064] Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum Arabic, talc, polyvinyl pyrrolidone, carpool gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of extracts and/or doses.

[0065] Pharmaceutical preparations that can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules contain the extract in admixture with fillers such as lactose, binders such as starches, and/or lubricants such as talc or magnesium separate and, optionally, stabilizers. In soft capsules, the extract may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols.

[0066] The dosage of BZL101 varies depending upon the tumor type, the stage of disease, the species of patient and the individual patient. In general, the amount of BZL101 administered to a human patient is equivalent to the soluble residue of about 0.1 g to about 1000 g of dried solid plant parts of BZL. In some embodiments, the effective dose is equivalent to about 1 to about 100 g of dried solid aerial plant parts of BZL, especially about 5 to about 50 g of dried solid aerial plant parts.

EXAMPLES

[0067] The herb from which the extracts of this invention were obtained were purchased from Shen Nong Herbs, Berkeley, California. Their identity was confirmed by reference to traditional pharmaceutical literature.

Preparative Example 1 – Preparation of BZL101 for *In Vitro* and Mouse Experiments

[0068] Herbal extract was prepared as "boiled teas", which is how most are prepared for use in traditional treatment regimes. Aqueous extracts were prepared by adding 7.5g of dry ground herb to 125 ml distilled water, bringing the mixture to a boil and then simmering for 45 minutes. The mixture was cooled, during which period most of the solids sank to the bottom of the vessel. The aqueous layer was carefully decanted off of the residual solids, centrifuged for 5 minutes at 1500 rpm, sterile filtered through a 0.45 μm filter and stored at 4°C until used. Generally, the extracts were tested within 1-2 weeks of preparation although most of the active extracts were found to retain activity after storage at 4°C for several additional weeks. An aliquot of each extract was dried under vacuum and the dry weight of the water soluble substances extracted from each herb determined.

Preparative Example 2 – Preparation of BZL101 for Human *In Vivo* Experiments

[0069] BZL101 is an aqueous extract of the aerial part of *Scutellaria Barbata* D. Don of the Lamiaceae family. Herba Scutellaria Barbata D. Don (Chinese pin yin transliteration- Ban Zhi Lian (BZL)) is grown

mainly in areas southeastern of the Yellow River (Huang Po) in the provinces of Sichuan, Jiangsu, Jiangxi, Fujian, Guangdong, Guangxi and Shaanxi. The plant is harvested in late summer and early autumn after it blooms. The aerial part (leaves and stems) is cut from the root and is used as starting material (BZL). The aerial part of the herb is dried in the sun, packed as a whole plant. The herb is identified and verified through botanical, morphological and chemical characteristics to ensure purity. A single dose of BZL101 is made through the following procedure and is termed BZL101 (Bionovo, Inc., Emeryville, CA).

- 180 grams of the raw herb is ground to fine powder (25 mesh)
- The powder is mixed with 1800 ml of distilled water to form a slurry
- The slurry is than simmered at 70-72°C for 60 minutes
- The extract is decanted and filtered through 22 μm filter
- The supernatant weight after extraction is 168 gm
- The volume of the solution is 1750 ml
- The extract is concentrated with a vacuum evaporator to reduce the volume of water to 350ml which constitutes a 5:1 concentration of the original solution
- The dry weight of soluble material in the extract is 12 gm
- It is packaged in a sterile, vacuum sealed container
- Testing for bacteria, yeast and heavy metals are preformed by an accredited laboratory

Comparative Example 1 -- *In vitro* Inhibition of Cancer Cell Activity

.Cell lines and culture

[0070] The extract obtained in Preparative Example 1, above, was tested against four human breast cancer cell lines, SKBR3, MFC-7, MDA-MB231 and BT474, and one murine breast cancer cell line, MCNeuA. All lines were maintained in 90% DME supplement with 2.0 mom L-glutamine, 100 IU/ml penicillin, 100 μg/ml streptomycin and 10% heat-inactivated fetal bovine serum. Cells at 70-80% confluence were used for plating for growth inhibition assays.

[0071] Cells were plated in 96-well flat bottom plates at 5,000 to 10,000 cells/well. The difference in number of cells plated adjusts for differences in the growth rates of these cell lines. Cells were allowed to adhere to the well walls overnight; then the extracts were added to triplicate wells at a 1:10 final dilution in culture medium for initial screening. For generating dose-response curves, serial 3-fold dilutions, starting at 1:10 dilution over 6 rows of wells were used. Water was added to the control wells at 1:10 dilution in culture medium. The plates were incubated at 37°C, 5% CO_2, for 3 days and then assayed for growth inhibition using a crystal violet assay (Bernhardt, G., et al., *Standardized Kinetic Microassay to Quantify Differential Chemosensitivity on the Basis of Proliferative Activity*, **1992**, J. Cancer Res. Clin. Oncol., 118:35-43). Cells remaining adherent to the well walls were rinsed with PBS, the fixed cells were stained with 0.02% aqueous crystal violet (50 μl/well) for 30 minutes after which the wells were washed thoroughly with distilled water. The crystal violet stain bound by the cells was solubilized in 79%

ethanol (100 µl/well) and the plates analyzed on a microplate reader (Molecular Devices) ay 595 nm. The percent inhibition was calculated as the average optical density of the control wells minus average optical density extract well divided by the average optical density of the control wells. Dose-response curves on SKBR3, MCF7 and MCNeuA cells for several of the extracts are shown in FIGs 1-3. As can be seen, the concentration at which the extracts inhibited the activity of the cells by 50% (the IC50) ranged from over 1 mg/ml down to about 10 µg/ml.

Induction of apoptosis

[0072] To assay for DNA fragmentation as a marker of apoptosis, a procedure for the isolation of genomic DNA that allows for the analysis of both high and low molecular weight DNA fragmentation during apoptosis was used. MCNeuA cells were plated at 5×10^5 cells/well in 6-plates and allowed to adhere overnight. Aqueous herbal extracts were added to each well at a 1:10 and a 1:50 dilution. Sterile water, diluted 1:10 in culture medium, was added to the control wells. After 24 hours, the cells were visually examined under a microscope and morphological changes noted. Attached and floating cells were harvested, washed with cold PBS and embedded in lysis buffer (50 mM NaCl, 20 mM Tris HCl, pH 8.0, 20 mM EDTA, 0.5% sodium sarkosyl, 50 µg/ml Rnase A and 100 µg/ml proteinase K) for 1 hour at 37°C. The cells were then washed with PBS and distilled water and placed in the wells of a conventional 1% agarose gel and electrophoresed overnight at approximately 1 V/cm. The gels were then stained with ethidium bromide and photographed under UV transillumination to give intense images. The images obtained are shown in Figure 4.

[0073] BZL101 was evaluated for antiproliferative activity on five breast cancer cell lines (SK-BR-3, MCF7, MDA-MB-231, BT-474, and MCNeuA). These cell lines represent important prognostic phenotypes of breast cancer expressing a range of estrogen and HER2 receptors. BZL101, tested at a 1:10 dilution (15μg/ ml), demonstrated >50% growth inhibition on four of the five cell lines (Campbell, 2002). BZL101 showed >50% growth inhibition on a panel of lung, prostate and pancreatic cancer cell lines. BZL101 at the same dose did not cause >25% of growth inhibition on normal human mammary cells (HuMEC), demonstrating selectivity to cancer cells (Table 3). Moreso, BZL101 had a mild mitogenic effect on normal human lymphocytes. In cell cycle analysis, BZL101 caused an S phase burst and G1 arrest. (See FIG. 8). BZL101 also attenuated mitochondrial membrane potential causing caspase-independent high molecular grade (HMG) apoptosis. (See FIG. 7).

[0074] The results of this *in vitro* experiment are summarized in Table 3, below.

Table 3

Lung		Pancreas		Prostate		Breast					
A549	LLC	Panc-1	Panc 02	PC-3	LNCaP	MCF7	BT474	SKBR3	MDA-MB-231	MCNeuA	HuMEC
+	+	+	++	+	+	++	+	++	+	++	-

[0075] Table 3: *In vitro* growth inhibitory effect of BZL101 aqueous extract of *Scutellaria Barbata* 1:10 dilution- < 50% inhibition, + 51-75% inhibition, ++ >75% inhibition. BZL is active on all cancer cell lines but is not active on HuMECs.

Example 1 – *In vivo* (IP) Efficacy of BZL101 in a Mouse Xenograft Model

[0076] In order to demonstrate the efficacy of BZL101 in the *in vivo* treatment of cancer, BZL101 was evaluated in a mouse xenograft model.

[0077] BZL101 was active via intraperitoneal (IP) administration in preventing tumor formation in a mouse xenograft model (FIG. 5). BZL101 was prepared as described in Preparative Example 1, above. Cells (10^5) of MCNeuA cells were injected subcutaneously into mice on day 0. BZL101 (0.5 ml or 1.0 ml) or control was administered to each mouse IP every two days. Tumor size (mm^3) was estimated on the 17^{th}, 21^{st}, 23^{rd}, 25^{th}, and 28^{th} day post administration. The results of this study, show in FIG. 5, demonstrate that BZL101 inhibited xenograft, suggesting that BZL101 can be an effective treatment for solid tumors *in vivo*.

Example 2 – *In vivo* (Oral) Efficacy of BZL101 in a Mouse Xenograft Model

[0078] In order to further evaluate the effect of the herb extract *in vivo*, BZL101 alone, BZL101 plus cyclophosphamide and cyclophosphamide alone were orally administered to mice having subcutaneous cancer xenografts.

[0079] As in Example 1, above, 10^5 cells were administered to each animal subcutaneously on Day 0. The animals were divided into four groups. The control group received only normal drinking water. The cyclophosphamide only group received 25 mg/Kg/day of cyclophosphamide in their drinking water. The BZL101only group received 0.5 ml of BZL101 by oral gavage on Day 0 and every third day after that. The combination group received 0.5 ml/day BZL101 by oral gavage on Day zero and every third day after that, as well as 25 mg/Kg/day of cyclophosphamide in their drinking water. The results of this experiment are shown in FIG. 6.

[0080] From the results in FIG. 6, it can be seen that, as expected, cyclophosphamide alone inhibited tumor growth as compared to the control. BZL101 alone also demonstrated tumor growth inhibition. And the combination of BZL101 and cyclophosphamide inhibited tumor growth to a greater extent than did either BZL101 or cyclophosphamide alone. These results demonstrate *in vivo* efficacy of BZL101 in the treatment of solid tumors and suggest that BZL101 is probably effective in the treatment of solid tumors in general.

Example 3 – Efficacy of BZL101 in Humans

[0081] In order to demonstrate the safety and clinical activity of oral BZL101, an aqueous extract from *Scutellaria Barbata* D. Don was studied in human patients with advanced breast cancer.

[0082] Eligible patients had histologically confirmed metastatic breast cancer and measurable disease. Patients did not receive any other chemotherapy, hormone therapy or herbal medicine during the trial. Patients received 350 ml (equivalent to 12 grams dry solubles BZL) BZL101 extract per day until disease progression, toxicity or personal preference caused them to discontinue. The primary endpoints were safety, toxicity and tumor response.

[0083] Twenty-one patients were enrolled and received BZL101. Mean age was 54 years (30 - 77) and mean number of prior treatments was 3.9 (0-10). There were no hematologic, nor grade III or IV non-hematologic, adverse events (AEs). Some patients reported grade I and II adverse events, such as nausea, diarrhea, headache, flatulence, vomiting, constipation, and fatigue. Sixteen patients were evaluable for response. Four of the 16 patients had stable disease (SD) for >90 days (25%) and 3/16 had SD for >180 days (19%). Five patients had minor objective tumor regression, one of which was 1 mm short of a PR based on RECIST criteria.

[0084] Patients were enrolled at the University of California, San Francisco Carol Franc Buck Breast Care Center and the Cancer Research Network in Plantation, Florida between August 2001 and November 2004 and signed an informed consent approved by local institutional review boards. All patients were ≥18 years old with histologically confirmed diagnosis of breast cancer and clinical evidence of metastatic involvement. Patients with solitary metastases required biopsy confirmation of metastatic disease. All patients had completed prior therapies and had adequate time to recover sufficiently from the toxicities associated with prior anticancer treatments. A life expectancy of 6 months and Karnofsky performance status of 80% or better was required. Nutritional or up to five times recommended daily allowance (RDA) vitamin supplementation were permitted; but concomitant use of non-study herbal agents was prohibited. Patients were excluded from the study for the following: extensive liver involvement (>50% of liver parenchyma), lymphangitic pulmonary involvement, central nervous system involvement or spinal cord compression not stabilized by therapy for >3 months, a history of multiple or severe food or medicine allergies and organ or marrow dysfunction as defined by creatinine >2.0 mg/dl, total bilirubin >1.7 mg/dl, white blood cell count <2,500 cells/μL and platelet count <75,000 mm^3.

[0085] Safety monitoring was done on a continuous basis and patients were seen by a physician for examination at baseline at every Y weeks. Adverse events were graded using Common Toxicity Criteria version 2, assigned a category by organ system and coded in relation to study drug as remote, possible, probably or definitely related. Baseline tumor assessments were done within 14 days of initiation of study drug and every three months. Responses were assessed using RECIST criteria. Study drug was administered at every visit, and at this visit compliance and a review of dosages taken was performed. BZL101 extract was provided as a liquid in a sealed and labeled aluminum packet containing a full daily dose that was administered in a split dose twice a day. Daily BZL extract was administered until the determination of tumor progression or dose limiting toxicity was encountered, or until the subject decided to voluntarily discontinue, in which case, the reason for discontinuation was obtained.

RESULTS

Patient Characteristics

[0086] A total of 22 patients with advanced breast cancer consented to the study and 21 patients were treated with at least one dose of oral BZL101 and included in the safety analysis. The last patient accrued to the study was not treated with BZL101 as funding for the study from the California Breast Cancer Research Program had ended and the expiration date for the study medication was nearing. Sixteen of the patients were treated for 28 days or more and evaluable according to the Response Evaluation Criteria in Solid Tumors (RECIST). Nine subjects discontinued study medication due to patient preference, and twelve patients were removed from the study due to progression based on RECIST criteria. None of the patients were removed from the study due to either grade III or IV adverse events categorized according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC) version 2. See Table 4 for a summary of study participants and Table 5 for a summary of selected patient characteristics.

Table 4: Summary of Study Participants

Study Participants Consented	22
Consented but not Treated with BZL101	1*
Included in Safety Analysis	21
Evaluable by RECIST Criteria	16
Off Study Due to Patient Preference	9
Off Study Due to Progression of Disease	12
Off Study Due to Grade III or IV Toxicity	0

*Inventory of study medication was nearing expiration and funding for the study had ended.

Table 5: Summary of Baseline Characteristics: Age, Height, Weight, Race or Ethnicity

Age	
Mean	54.3 years
Median	55.5 years
Range	30-77 years
Height	
Mean	65.2 inches
Median	65.0 inches
Range	62-68 inches
Weight	
Mean	137.1 pounds
Median	139 pounds
Range	108-165 pounds
Race or Ethnicity	
Caucasian	13 (59%)
African American	2 participants (9%)
Hispanic	1 participant (5%)
Asian	1 participant (5%)
Native American	1 participant (5%)
Unknown	4 participants (18%)

Safety Data

[0087] There were no deaths, serious adverse events or hematological adverse effects attributed to the study medication BZL101. There were no grade III or IV toxicities that were classified as possibly, probably or definitely related to BZL101.

Efficacy

[0088] Of the 21 patients who were treated with study medication, 16 patients were on the trial for 28 days or more and evaluable for response. Four of the 16 patients (25%) had stable disease for >90 days and 3/16 (19%) had stable disease for >180 days. Five patients had some degree of objective tumor regression, classified as a minimal response (<10% but <30 reduction in diameter sums). One of these responses was 1 mm short of a partial remission based on RECIST criteria. The average number of prior therapies for metastatic disease prior to treatment with the study medication, for patients who took at least one dose of BZL101, was 3.9 (See Table 6).

Table 6: Response to Treatment Based on RECIST Criteria

Patient #	Age	On Study	Days on Study	Reason for Discon-tinuation	Prior Therapies After Diagnosis of Metastasis But Before BZL101	Recist Criteria (Months) NE=Not evaluable PD=Progressive Disease, SD=Stable Disease, PR=Partial Remission, CR=Complete Remission MR=Minimal Response, >0% and <30%reduction					
						NE	PD	SD	PR	CR	MR
2001	48	08/28/01 - 03/14/02	184	Progression	CMF Capecitabine		6	3			
2002	30	10/02/01 - 10/26/01	25	Progression	Goserelin Anastrozole Tamoxifen Targretin trial Docetaxel AC High dose chemo Capecitabine VEGF Trial Exemestane		<1				
2003	50	10/30/01 - 04/17/02	151	Pt Preference	Anastrozole Tamoxifen			5			2,3,4
2004	77	12/20/01 - 09/05/02	259	Progression	None		9	6			3
2005	64	03/07/02 - 04/11/02	36	Pt Preference	None			1			

Patient #	Age	On Study	Days on Study	Reason for Discon-tinuation	Prior Therapies After Diagnosis of Metastasis But Before BZL101	Recist Criteria (Months) NE=Not evaluable PD=Progressive Disease, SD=Stable Disease, PR=Partial Remission, CR=Complete Remission MR=Minimal Response, >0% and <30%reduction					
						NE	PD	SD	PR	CR	MR
2006	59	10/31/02 - 01/09/03	71	Pt preference	CAF Tamoxifen CMF Paclitaxel Carboplatin + Etoposide Capecitabine	NE					
2007	60	12/09/02 - 12/25/02	16	Pt Preference	Docetaxel Trastuzamab Cisplatin Capicitabine Liposomal doxirubicin Gemcitabine	NE					
2008	52	06/24/03 - 08/21/03	59	Pt Preference	Exemestane Tamoxifen Capecitabine	NE					
2009	34	09/12/03 - 10/28/03	41	Progression	Doxorubicin Paciltaxel Docetaxel		1.5				
2010	56	06/26/03 - 06/27/03	1	Pt Preference	Tamoxifen CAF Traztuzamab Gemcitabine Letrozole Fulvestrant	NE					
2011	48	04/21/04 - 07/23/04	93	Progression	Docetaxil Gemcitabine		3				
2012		11/08/04 - 11/15/04	6	Pt Preference	Letrozole Fulvestrant Carboplatin + Docetaxel Zoledronic acid	NE					
3001	54	02/28/02 - 04/19/02	51	Progression	Vinorelbine Traztuzamab Capecitabine		1.5				
3002	48	02/28/02 - 03/07/02	7	Pt Preference	Anastrazole Letrazole	NE					
3003	59	03/01/02 - 11/15/02	260	Progression	Liposomal doxorubicin +Paclitaxel		9				1

Patient #	Age	On Study	Days on Study	Reason for Discon-tinuation	Prior Therapies After Diagnosis of Metastasis But Before BZL101	Recist Criteria (Months) NE=Not evaluable PD=Progressive Disease, SD=Stable Disease, PR=Partial Remission, CR=Complete Remission MR=Minimal Response, >0% and <30%reduction					
						NE	PD	SD	PR	CR	MR
3004	59	03/04/02 - 04/06/02	33	Progression	Tamoxifen Docetaxel Letrazole						1
3005	60	03/29/02 - 05/12/02	42	Progression	Tamoxifen Letrozole Anastrozole Vinorelbine + Capecitabine NFL		1				
3006	56	04/17/02 - 07/01/02	63	Progression	Tamoxifen Liposomal doxorubicin NFL Anastrozole Trastuzamab Vinorelbine Gemcitabine Capecitabine		2				1
3007	54	09/13/02 - 11/11/02	59	Progression	TAC Tamoxifen Doxorubicin Trastuzamab Docetaxel CMF Vinorelbine Capecitabine Fulvestrant		2				
3008	67	04/09/04 - 05/17/04	38	Pt Preference	Paclitaxel Vinorelbine + Capecitabine Pfizer clinical trial Docetaxel Gemcitabine Liposomal doxorubicin			1			
3009	45	05/24/04 - 08/27/04	95	Progression	None		3				

Patient #	Age	On Study	Days on Study	Reason for Discon-tinuation	Prior Therapies After Diagnosis of Metastasis But Before BZL101	Recist Criteria (Months) NE=Not evaluable PD=Progressive Disease, SD=Stable Disease, PR=Partial Remission, CR=Complete Remission MR=Minimal Response, >0% and <30%reduction					
						NE	PD	SD	PR	CR	MR
3010	59	Not treated	0		Tamoxifen Anastrozole Capecitabine Vinorelbine Liposomal doxorubicin+ Gemcitabine Carboplatin + Paclitaxel Fulvestrant Toremifene Letrozole Zoledronic Acid	NE					

NFL mitoxantrone, 5-fluorouracil, leucovorin
CMF cyclophosphamide, methotrexate, fluorouracil
CAF cyclophosphamide, adriamycin, fluorouracil
TAC docetaxel, adriamycin (doxorubicin), cyclophosphamide
AC adriamycin (doxorubicin),cyclophosphamide

[0089] In a modified RECIST evaluation, where all measurable lesions were included as evaluable, one patient had a partial response or a reduction of 31% in the sum of the longest tumor diameter of all measurable lesions after 7 weeks of treatment and a reduction of 33% after 11 weeks of treatment (Table 7).

Table 7: Patient #2003 Response to Treatment Based on Modified RECIST Criteria

DATE	**Lesion 1 Site and Method**	**Lesion 2 Site and Method**	**Lesion 3 Site and Method**	**Lesion 4 Site and Method**	**Total Measurable Disease**
	Measurement	**Measurement**	**Measurement**	**Measurement**	
#2003 **Baseline** 10/30/01	**Site**: Lymph Node-Left Subclavian **Method**: Palpation **Measurement**: 3.0 x 2.5 cm	**Site**: Lymph Node-Anterior Cervical **Method**: Palpation **Measurement**: 2.0 x 2.0 cm	**Site**: Lymph Node-Left Subclavian, Post Cervical **Method**: Palpation **Measurement**: 0.8 cm	**Site**: Vertebrae/Pelvis **Method**: Pelvic CT scan Bony metastases	**Total Baseline Diameters = 5.8 cm**

Month 2 12/20/01	**Measurement:** 2.0 x 2.0 cm	**Measurement:** 1.5 x 1.0 cm	**Measurement:** 0.5 cm	**Site:** Bone **Method:** Bone Scan Bony Mets	**Total Sum = 4.0 cm % Change= -31%**
Month 3 01/22/02	**Measurement:** 2.1 x 1.5 cm	**Measurement:** 1.5 x 1.2 cm	**Measurement:** 0.3 cm	**Site:** Bone **Method:** Bone Scan Bony mets grossly stable compared with 11/19/01	**Total Sum = 3.9 cm % Change = -33%**
Month 4 03/08/02	**Measurement:** 2.0 x 1.5 cm	**Measurement:** 2.0 x 2.0 cm	**Measurement:** 0.5 cm		**Total Sum = 4.5 cm % Change = -24%**
Month 5 04/17/02	**Measurement:** 3.0 x 2.5 cm	**Measurement:** 2.0 x 1.5 cm	**Measurement:** 0.5 cm		**Total Sum = 5.5 cm % Change = -5%**

CONCLUSION

[0090] The herbal extract BZL101, its uses for the inhibition of solid tumor cancer cells and the treatment of such cancers in patients are described herein. Although certain embodiments and examples have been used to describe the present invention, it will be apparent to those skilled in the art that changes to the embodiments and examples may be made without departing from the scope and spirit of this invention.

[0091] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising a therapeutically effective amount of an aqueous extract of *Scutellaria barbata* and a pharmaceutically acceptable excipient.

2. The pharmaceutical composition of claim 1, wherein the extract of *Scutellaria barbata* reduces the activity of at least one cancer cell line *in vitro*.

3. The pharmaceutical composition of claim 2, wherein the cancer cell line inhibited by the extract is selected from a SKBR3 cell, a MCF7 cell, a MDA-MB231 cell, a BT474 cell or a MCNeuA cell (breast cancer cells), A549 cell, LLC cell (Lung Cancer cells), Panc1 cells, Panc02 cells (Pancreatic cancer cells), PC-3 cells LNCaP cells (Prostate Cancer cells), OVCAR cells, and SKOV3 cells (Ovarian Cancer cells).

4. The pharmaceutical composition of claim 3, wherein the extract of *Scutellaria barbata* induces apoptosis in at least one cancer cell line.

5. The pharmaceutical composition of claim 4, wherein the cancer cell line in which apoptosis is induced by the extract is selected from a SKBR3 cell, a MCF7 cell, a MDA-MB231 cell, a BT474 cell, a MCNeuA cell (breast cancer cells), A549 cell, LLC cell (Lung Cancer cells), Panc1 cells, Panc02 cells (Pancreatic cancer cells), PC-3 cells LNCaP cells (Prostate Cancer cells), OVCAR cells, and SKOV3 cells (Ovarian Cancer cells).

6. The pharmaceutical composition of claim 1, wherein the extract of *Scutellaria barbata* induces cell growth arrest in the G1 state *in vitro*.

7. The pharmaceutical composition of claim 6, wherein the cancer cell line in which cell growth arrest in the G1 state is selected from the group consisting of a SKBR3 cell, a MCF7 cell, a MDA-MB231 cell, a BT474 cell or a MCNeuA cell (breast cancer cells), A549 cell, LLC cell (Lung Cancer cells), Panc1 cells, Panc02 cells (Pancreatic cancer cells), PC-3 cells LNCaP cells (Prostate Cancer cells), OVCAR cells, and SKOV3 cells (Ovarian Cancer cells).

8. A method of inhibiting cancer in a mammal, comprising administering to the mammal a therapeutically effective amount of an extract of *Scutellaria barbata*.

9. The method of claim 8, wherein the cancer is a xenograft selected from SKBR3, MCF7, MDA-MB231, BT474, MCNeuA, A549 cell, LLC, Panc1, Panc02, PC-3, LNCaP, OVCAR and SKOV3.

10. The method of claim 9, wherein the mammal is a mouse.

11. The method of claim 8, wherein the cancer is an epithelial cancer.

12. The method of claim 11, wherein the epithelial cancer is breast or ovarian cancer.

13. The method of claim 8 or 12, wherein the mammal is a human.

14. A method of inducing apoptosis in a cancer in a mammal, comprising administering to the mammal a therapeutically effective amount of an extract of *Scutellaria barbata.*

15. The method of claim 14, wherein the cancer is a xenograft selected from SKBR3, MCF7, MDA-MB231, BT474, MCNeuA, A549 cell, LLC, Panc1, Panc02, PC-3, LNCaP, OVCAR and SKOV3.

16. The method of claim 15, wherein the mammal is a mouse.

17. The method of claim 16, wherein the cancer is an epithelial cancer.

18. The method of claim 17, wherein the epithelial cancer is breast or ovarian cancer.

19. The method of claim 14 or 18, wherein the mammal is a human.

20. A method of arresting growth in the G1 state of a cancer in a mammal, comprising administering to the mammal a therapeutically effective amount of an extract of *Scutellaria barbata*.

21. The method of claim 20, wherein the cancer is a xenograft selected from SKBR3, MCF7, MDA-MB231, BT474, MCNeuA, A549 cell, LLC, Panc1, Panc02, PC-3, LNCaP, OVCAR and SKOV3.

22. The method of claim 21, wherein the mammal is a mouse.

23. The method of claim 20, wherein the cancer is an epithelial cancer.

24. The method of claim 23, wherein the epithelial cancer is breast or ovarian cancer.

25. The method of claim 20 or 24, wherein the mammal is a human.

26. A method of treating cancer, comprising administering to a patient an amount of a pharmaceutical composition comprising an extract of *Scutellaria barbata* D. Don effective to treat said cancer.

27. The method of claim 26, wherein the cancer is a solid cancer.

28. The method of claim 27, wherein the solid cancer is an epithelial cell cancer.

29. The method of claim 28, wherein the epithelial cell cancer is breast cancer or ovarian cancer.

30. The method of claim 26, wherein said treatment reduces the rate of growth of the cancer.

31. The method of claim 26, wherein the treatment reduces the size of the cancer.

32. The method of claim 26, wherein the treatment induces remission of the cancer.

33. The method of claim 26, wherein the pharmaceutical composition is an oral composition.

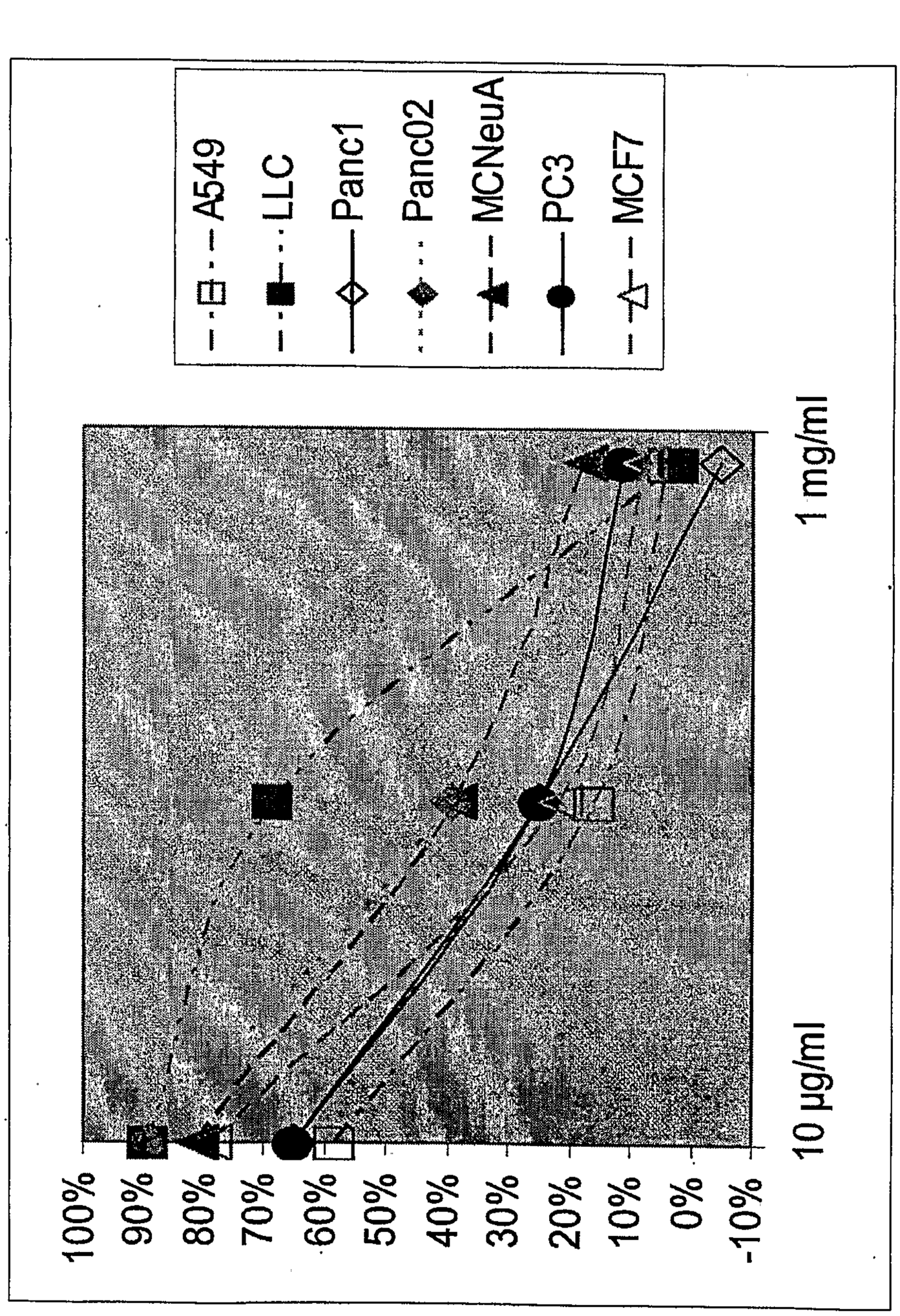


Figure 1
Dose-response curves showing the response of several solid cancer tumor cells to BZL100.

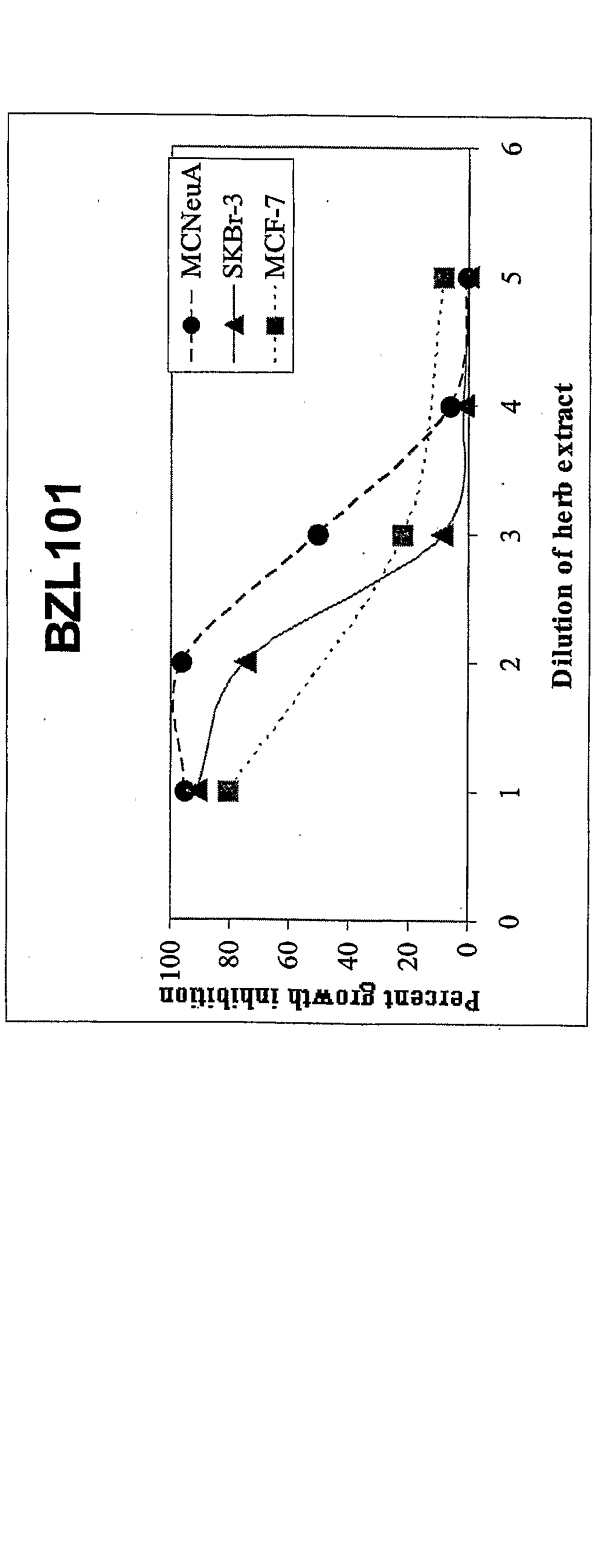


Figure 2.

Dose-response curves showing the response of breast solid cancer tumor cells to BZL101.

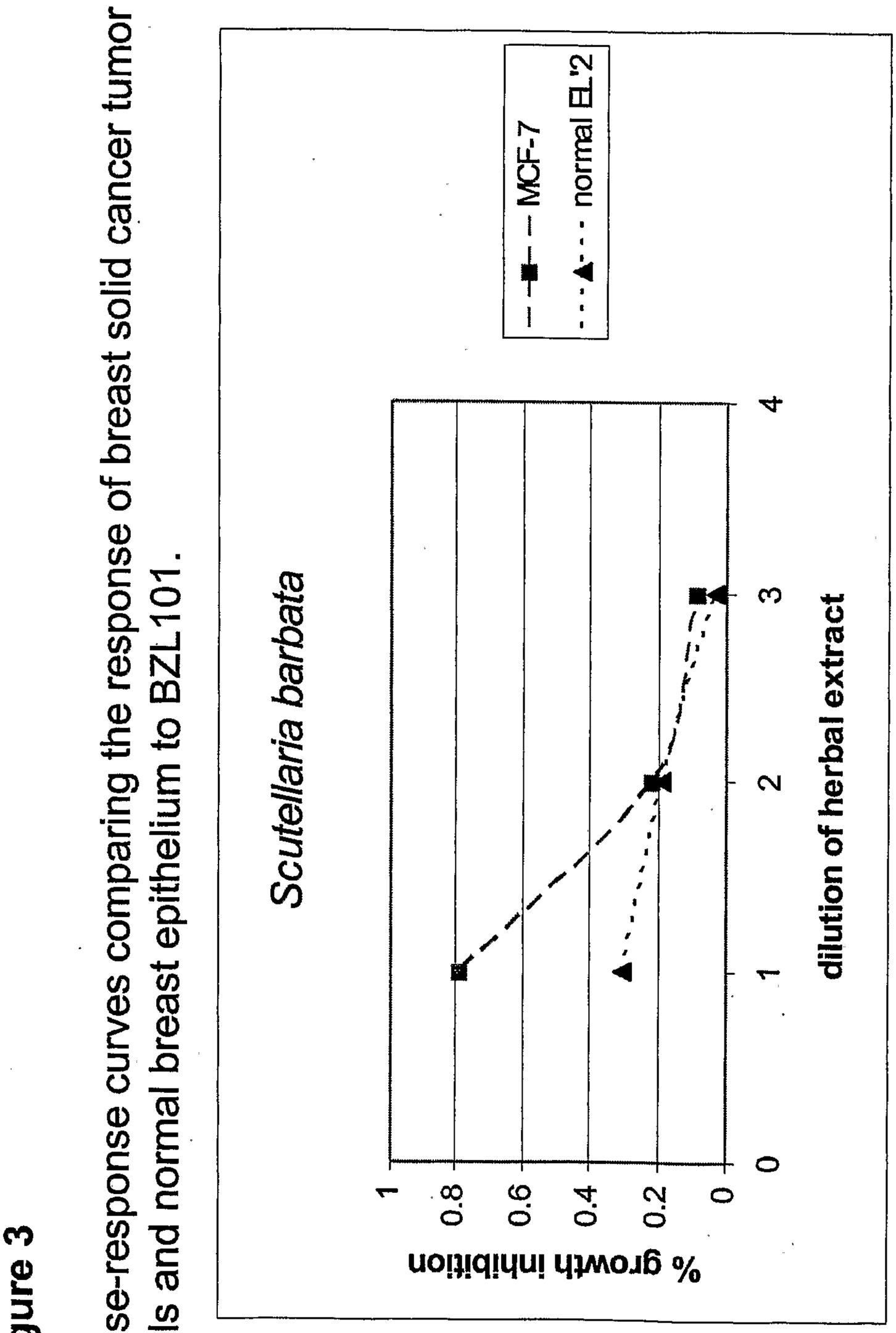

Dose-response curves comparing the response of breast solid cancer tissue cells and normal breast epithelium to BZL101.
Scutellaria barbata
MCF-7
normal EL'2
% growth inhibition
1
0.8
0.6
0.4
0.2
0
0
1
2
3
4
dilution of herbal extract

Figure 3

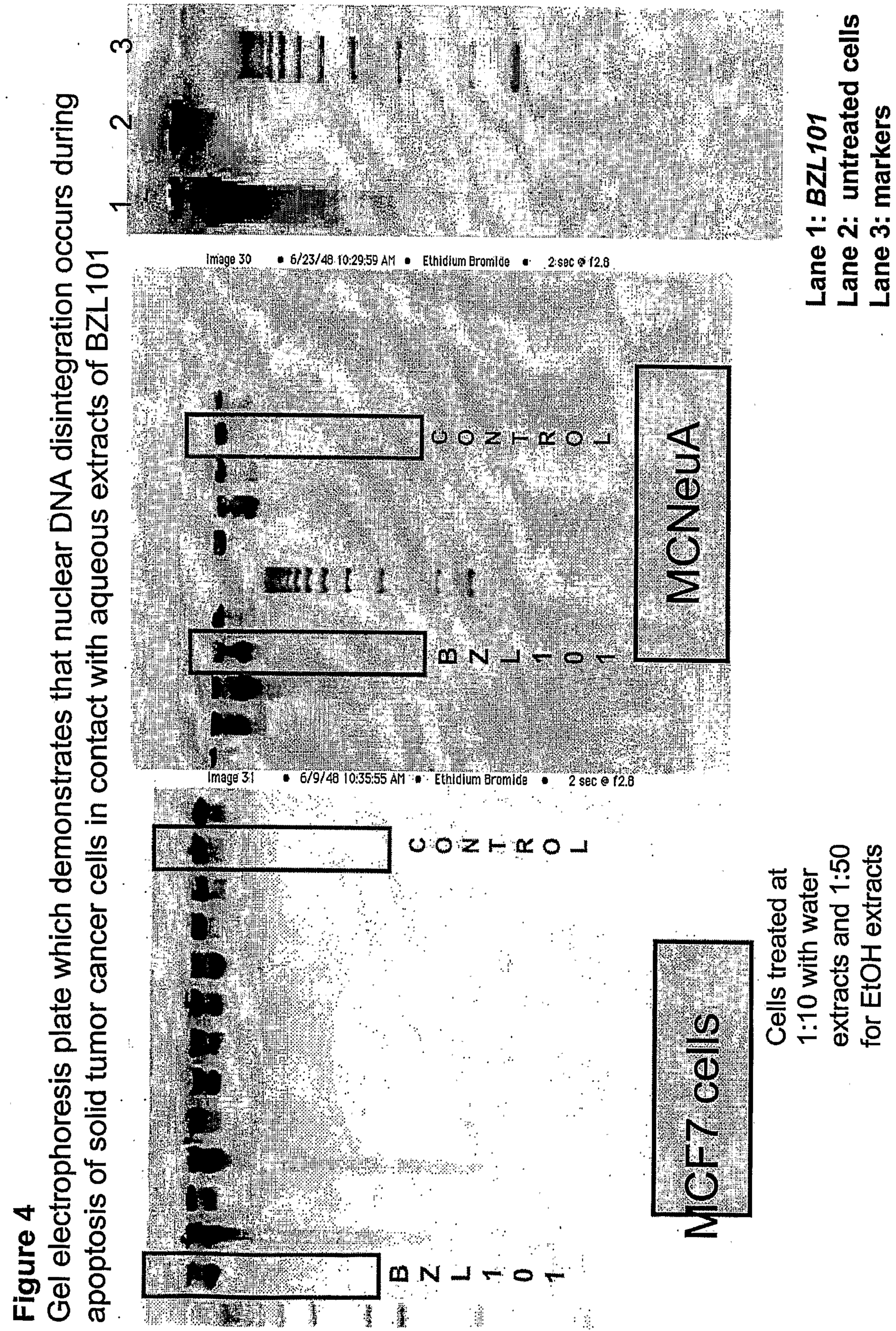
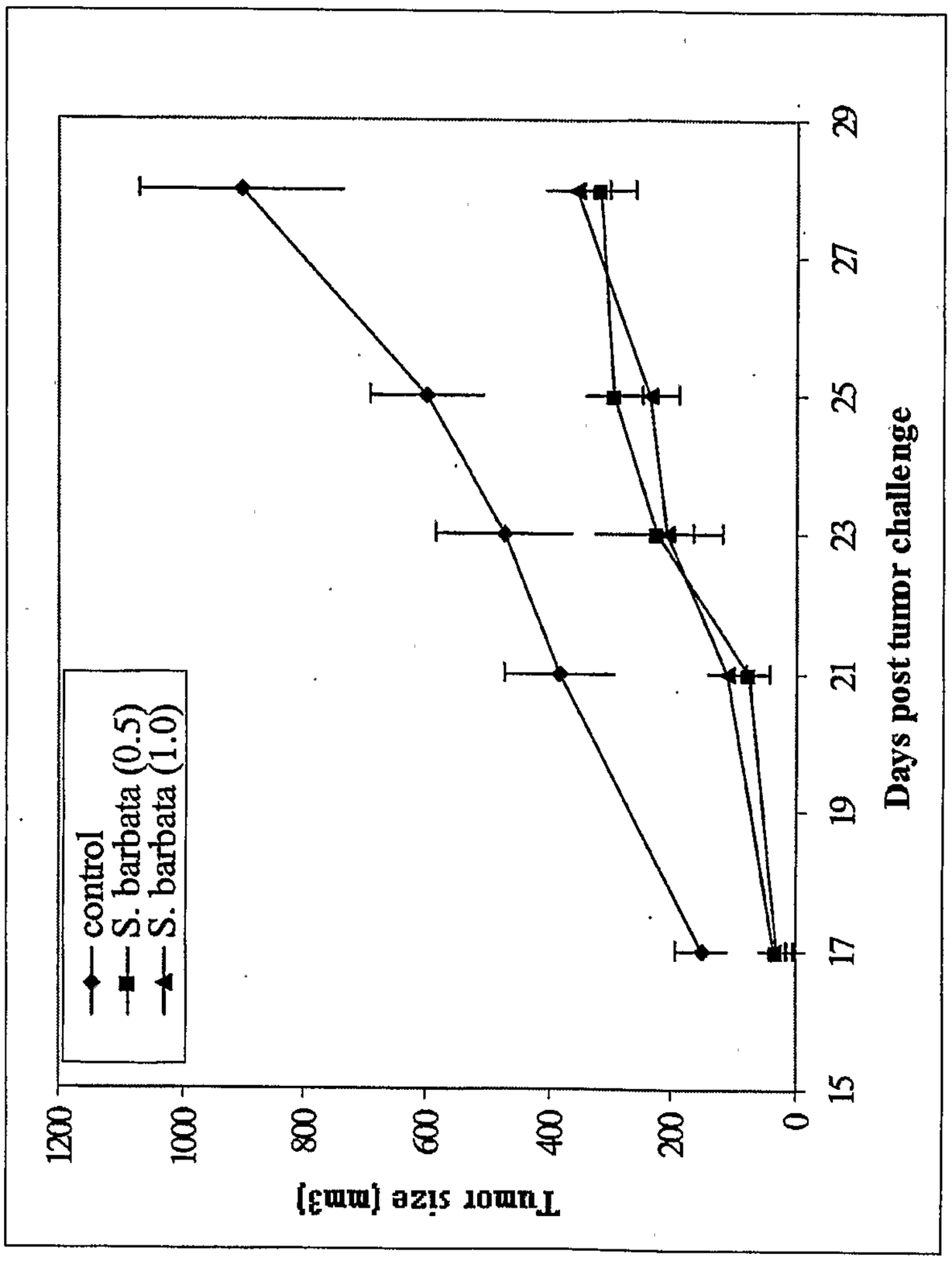


Figure 4
Gel electrophoresis plate which demonstrates that nuclear DNA disintegration occurs during apoptosis of solid tumor cancer cells in contact with aqueous extracts of BZL101

Figure 5

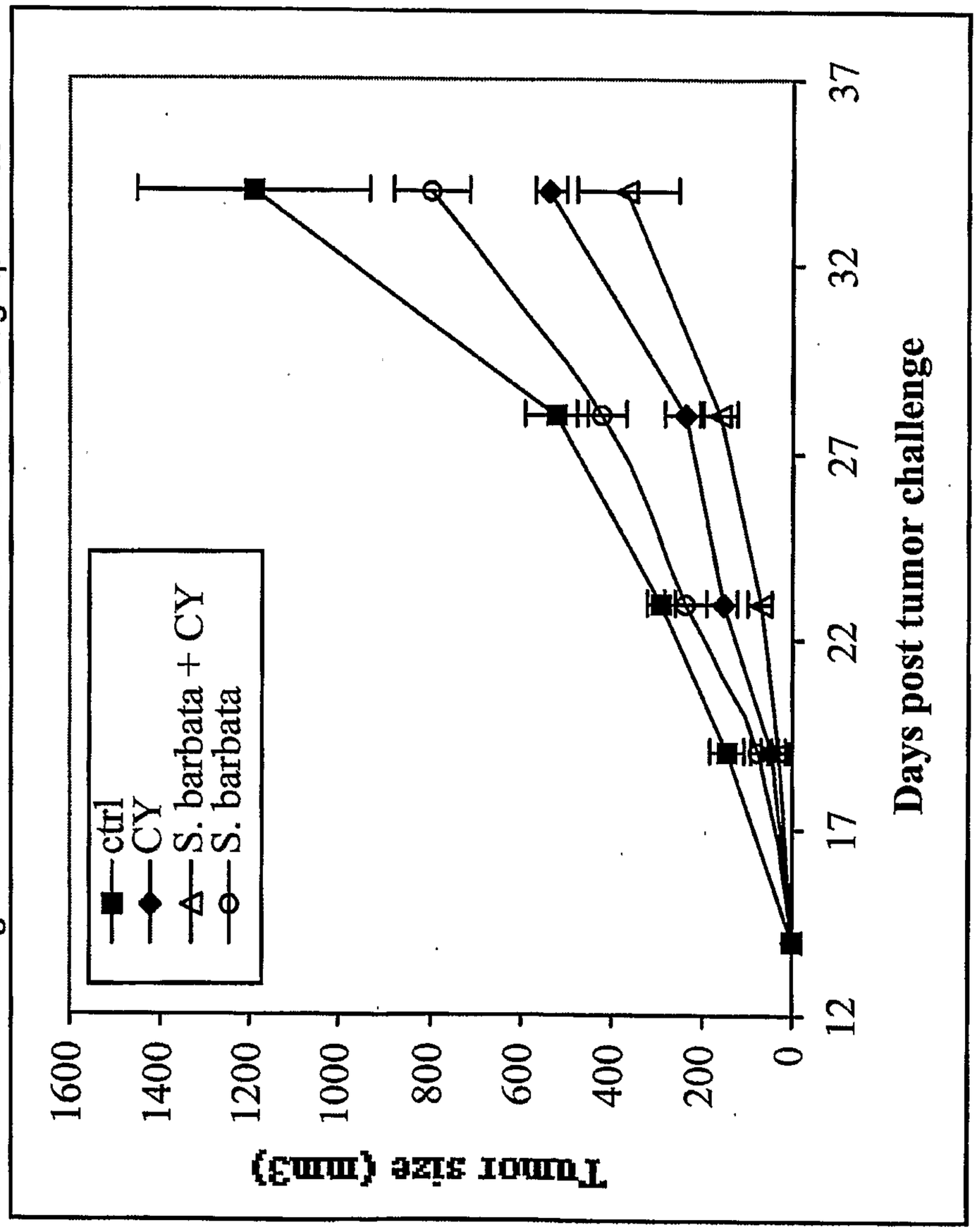
BZL101 administered intraperitoneially (IP) reduces the growth of xenograft tumors in a mouse model.



- Day 0 – 10^5 MCNeuA tumor cells, sc
- Herbs – 0.5 ml or 1.0 ml per mouse, i.p., every 2 days beginning day 0

Figure 6

The effect of the BZL101 administered by oral gavages and in interaction with cyclophosphamide administered in low dose in the drinking water on the tumors of mice in a xenograph model.



- Day 0 -- 10^5 tumor cells, sc
- CY -- ~25 mg/kg/day, orally, beginning day 0
- Herb -- 0.5 ml/mouse, every 3 days, beginning day 0

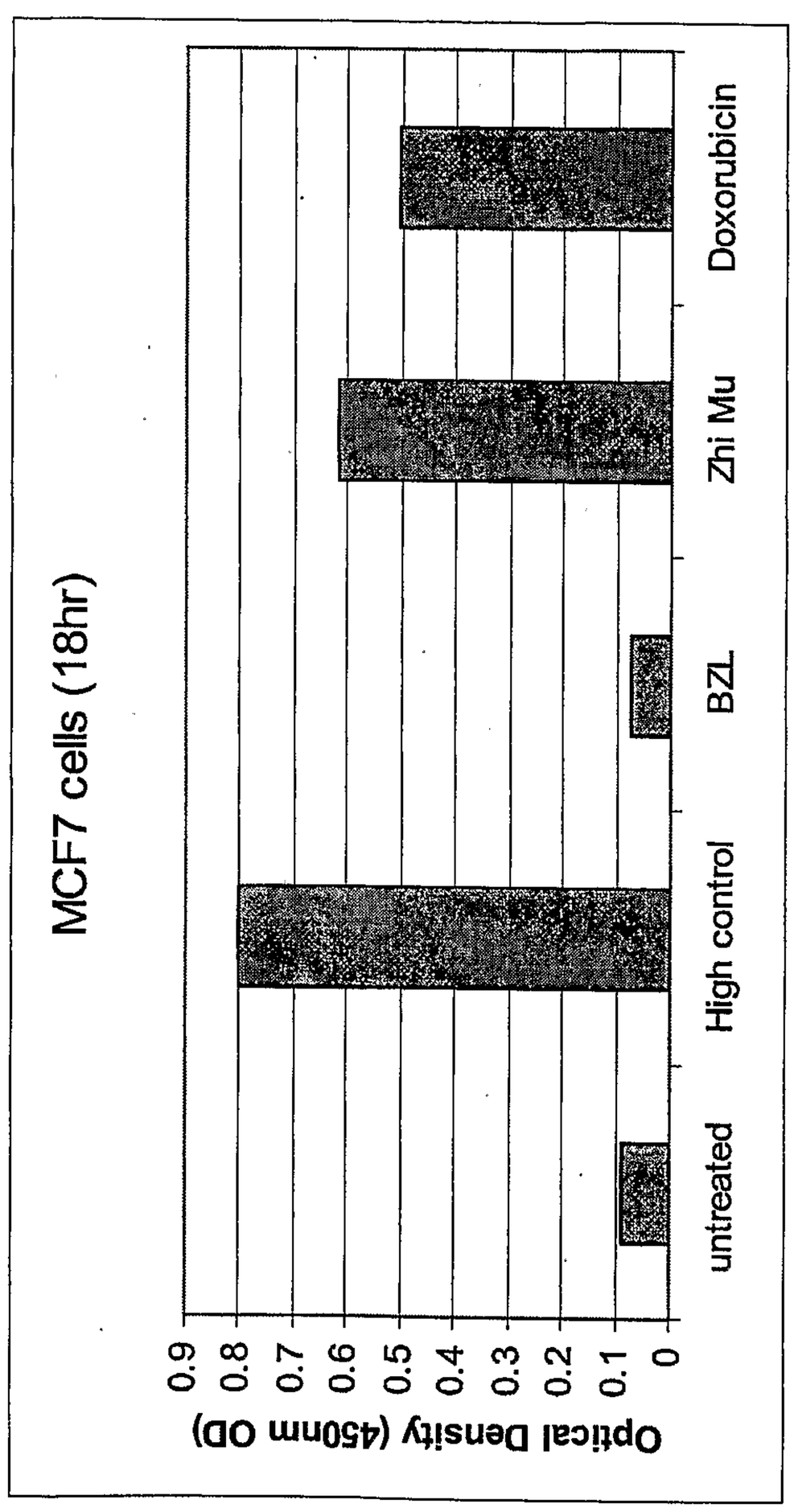
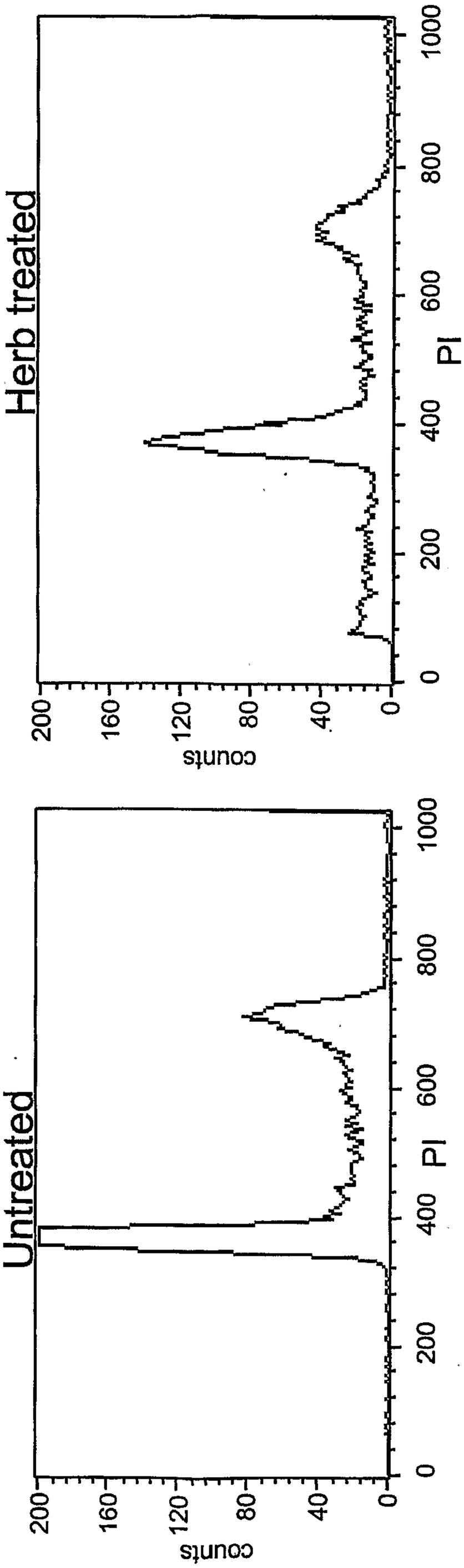

BZL101 induces apoptosis without activating caspases
MCF7 cells (18hr)
Optical Density (450nm OD)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
untreated
High control
BZL
Zhi Mu
Doxorubicin
BZL101 Does Not Induce Caspase Activation (CK18 cleavage assay)

Figure 7

Figure 8

BZL101 in cell cycle analysis arrests the cells at the G1 phase.



	G1	S	G2/M	apoptosis
Untreated control	36.9%	45.3%	17.8%	8.8%
S. barbata			19.4%	

BZL101 arrests breast cancer cells in the G1 phase of the cell cycle and induces apoptosis as measured by a sub-G1 population of cells