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(54) Title: NATURAL PRODUCT COMPOSITION FOR USE IN TREATING CANCER

(57) Abstract

The present invention relates to a novel method and pharmaceutical compositions for use in combatting cancer comprising ingesting and/or applying a composition prepared by extracting one or more plants selected from the group consisting of Centaurea, Capsicum, Sambucus, Lobelia, Myrrh, Echinacea, Goldenseal, and Myrtle. While extracts of one or more of these plants were found to be active against cancers resistant to known anti–cancer agents, activity against cancer has also been found with the extension of specific binary and three–way mixtures of the above described plants as well as mixtures of all the plants.

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NATURAL PRODUCT COMPOSITION FOR USE IN TREATING CANCER

FIELD OF THE INVENTION

The present invention concerns novel compositions and their health and medical use. The present invention more particularly concerns a novel composition containing natural ingredients which heighten the activity of a patient's immune system and can be used to treat a large variety of cancers.

BACKGROUND OF THE INVENTION

Cancer is a disease of abnormal cell growth which often leads to death. Cancer is generally treated by three principal means: surgical removal of a tumor, therapeutic radiation or treatment with drugs, such as antitumor compounds. There are numerous drugs which are used to combat a large variety of cancers. However, these drugs are made of individual or combinations of chemicals. While some are effective, many have side effects, especially cytoxicity, which prevent their long-term or recurrent use. In addition, there has been an increasing number of effective drugs which can no longer be used due to the resistance by the causative agent.

SUMMARY OF THE INVENTION

The present invention relates to a novel method and pharmaceutical compositions for use in combatting cancer comprising administering (preferablly, orally or topically) a composition prepared by extracting one or more plants selected from the group consisting of Centaurea, Capsicum, Sambucus, Lobelia, Myrrh, Echinacea, Goldenseal, and Myrtle. While extracts of one or more of these plants were found to be active against cancers resistant to known anti-cancer agents, activity against cancer has also been found with the extension of specific binary (two plant) mixtures and three-way mixtures of the above described plants as well as mixtures of all the plants as will be detailed below.

BRIEF DESRIPTION OF THE FIGURES

Figure 1 shows the cytotoxic effects of plant extracts on HCT-8 colon tumor cells.

Figure 2 shows the cytotoxicity of plant extracts in different human tumor cells and normal fibroblast cells.

Figure 3 shows the cytotoxicity of plant extracts in non-tumor CMH-F1 skin fibroblast cells.

Figure 4 shows the cytotoxic effects of plant extracts in drug sensitive SW 1573 lung cancer cells.

Figure 5 shows the cytotoxic effects of plant extracts in multi-drug resistant SW 1573-2R160 lung cancer cells.

Figure 6 shows the *in vitro* effects of plant extracts on fresh tumor cells derived from individual patients.

The key or legend to figures 1-6 is as follows:

G	=	Goldenseal
A	=	Centaurea
B	=	Capsicum
C	=	Sambucus
D	=	Lobelia
E	=	Myrrh
F	=	Echinacea
H	=	Myrtle

DETAILED DESCRIPTION OF THE INVENTION

The term "cancer" is used throughout the specification to refer to the pathological process that results in the formation and growth of a malignant neoplasm, i.e., abnormal tissue that grows by cellular proliferation, often more rapidly than normal and continues to grow after the stimuli that initiated the new growth cease. Malignant neoplasms show partial or complete lack of structural organization and functional coordination with the normal tissue and most invade surrounding tissues, metastasize to several sites, and are likely to recur after attempted removal and to cause the death of the patient unless adequately treated. As used herein, the term cancer is used to describe all cancerous disease states and embraces or encompasses the pathological process associated with malignant hematogenous, ascitic and solid tumors.

The term "anticancer effective amount" is used throughout the specification to describe an amount of the present composition which is used to "combat cancer", i.e., to treat a patient suffering from cancer including a cancerous tumor through one or more of the following mechanisms: by inhibiting the growth of the cancer as well as inhibiting the progression or metastasis, by preventing the further growth of the cancer, bringing that growth under control and preferably, producing a remission of the cancer and/or tumor.

The term "initially" is used to describe plants which are preferably extracted, then mixed. It is noted in the present invention that plants are preferably extracted and the extracts combined. Alternatively, individual plants may be combined and then extracted to produce products without further combination , essentially within the same relative weight ratios which are used to extract a mixture of plants.

Binary mixtures containing goldenseal, myrtle, and centaurea when each plant is initially present in the proportion of 3:1 to 1:3 have been found to be active. The plants in the referred three-way mixture are initially present in the following percenatges by weight:

(a) 30% to 70% Goldenseal

(b) 20% to 40% Myrtle and

(c) 5% to 20% Centaurea

Preferable, initial percentages of this mixture are 35% to 65% ; 25% to 35% and 7% to 15%, respectively.

The eight way mixture of plants according to the present invention initially contains the following percentages by weight:

(a) 3% to 5% Centaurea

(b) 1.5% to 4% Capsicum

(c) 1.5% to 3% Sambucus

(d) 1.5% to 4% Lobelia

(e) 20% to 40% Myrrh

(f) 30% to 50% Echinacea

(g) 15% to 25% Goldenseal

(h) 3% to 5% Myrtle

Preferable initial percentages of this mixture are 2% to 4% Centaurea, 2% to 3% Capsicum, 2% to 3% Sambucus; 2% to 3% lobelia; 25% to 35% Myrrh; 35% to 45% Echinacea; 18% to 22% Goldenseal; and 3.5% to 4.5%, respectively. Optionally, Burdock may be added to the eight-way mixture in amounts ranging from 2% to 5% by weight of the composition and/or Saffron in an amount ranging from 0.5% to 1% by weight of the composition.

While the plants or their mixtures may be extracted with any convenient solvent, preferred solvents are water or ethyl alcohol or a mixture of water and ethanol. The novel compositions are readily prepared by adding, preferably for example, water to the dry plant or mixtures of plants in a suitable container in an amount equal to approximately four times the weight of the dry mixture, bringing to a boil (or at least to a temperature of 70°C, boiling/heating for a short while (ie., about 10 minutes or so) and adding to the cooled water

solution (at a temperature less than the boiling point of alcohol) sufficient ethyl alcohol to result in an alcohol content of the diluted solution equal to 10% to 30% ethyl alcohol by volume. The thus obtained mixture is preferably allowed to stand for two weeks, stirring occasionally. The resulting mixture is filtered twice and bottled. The amount of solvent used may vary, and may be significantly less where ethyl alcohol is used alone. It is to be understood that the portions of the plants used for extraction are those which have been conventionally used. In certain instances, it may be appropriate to use the whole plant or parts of the plant, for example, the roots, stems or leaves.

When ethyl alcohol or a mixture of water and ethyl alcohol are used as extraction liquids (at a weight ratio of about 0.5:1 to about 8:1 by weight of the plants to be extracted, more preferably about 4:1), there is no need for the step of adding additional alcohol. The thus obtained tincture can be used by adding directly to liquids or other foods. Alternatively, the tincture may be evaporated to form a powder, which can be mixed with foods or alternatively, placed in capsules either alone or in combination with pharmaceutically acceptable excipients and the like.

The compositions of the present invention in the form of extracts of the individual plants or their mixtures have shown unusual and unexpected activity against cancer cells such as colon, leukemia, and the like. Such cells were killed in at least 3 of 7 samples, even at a dilution of 200 times. Other cancers to be treated by the present compositions include, for example, skin cancer, prostate cancer, bladder cancer, hepatocellular cancer, breast cancer, ovarian cancer, lymphoma, lung cancer, nasopharangeal cancer and pancreatic cancer, among others.

The amount of compound included within the therapeutically active formulations according to the present invention is an effective amount for treating the cancer (an anti-cancer effective amount). The dosage required to obtain a satisfactory response depends on the circumstances and will vary according to the desired effect, the difficulty of treating the cancer involved and the pervasiveness of the cancer. It will also depend upon whether a

liquid or a solid composition (in the form of a powder) is to be used. In the case of a liquid composition, the amount of liquid (as water, ethanol or a water/ethanol mixture) will preferably range from about 15% to about 45% by weight of the final composition. Obviously, the routineer can readily modify the formulation to make it stronger (with less liquid) or weaker/more dilute (more liquid). Generally (when the amount of liquid ranges from 15% to 45% by weight of the composition), a dose of 10 to 40 drops (approximately 1.25 ml to 2.5 ml) 4 to 6 times a day is preferred. A more preferred dose for most cases is 15 to 30 drops, with 30 drops for adults and 15 drops for children up to age 12. In the case of the powder, an amount of material preferably ranging from approximately 1/4 to 4 teaspoons a day may be used, with a more preferred amount being approximately 2 teaspoons. The composition is preferably administered at least twice a day (BID), more preferably four times a day (QID) or more. The routineer will recognize that the amount of the present composition to be administered to a patient may be varied widely.

One of ordinary skill in the art will recognize that a therapeutically effective amount of the composition according to the present invention to be used to treat or combat cancer, including malignant tumors will vary with the disease state or condition to be treated, its severity, the treatment regimen to be employed, the result desired (for example, remission or the shrinkage of a tumor), the type of administration used to deliver the compounds, as well as the patient (animal or human) treated.

In the pharmaceutical aspect according to the present invention, the composition according to the present invention is used alone, but may be formulated in admixture with a pharmaceutically acceptable additive, carrier or excipient. In general, it is preferable to administer the pharmaceutical composition topically or orally, but consideration should be given to other formulations administered via intramuscular, transdermal, buccal, subcutaneous, suppository or other route. Of course, one of ordinary skill in the art may modify the formulations within the teachings of the specification to provide numerous formulations for a particular route of administration.

While the invention will now be described in connection with certain preferred embodiments in the following examples, it will be understood that it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims.

EXPERIMENTAL- GENERAL

Test Subtances

Plant extracts were tested for cytotoxic effects in cultured cell lines. All examples were ethanol extracts of the plant leaves with a final alcohol concentration of 16%-41% (vol/vol), mean of 24%. All plant extracts were supplied in dark glass bottles and stand at room temperature.

Cell Culture

The following human cancer cell lines were used; colon (HCT8, COLO201, SW 837); lung (SW1573, SW1573-2R160). The cells were obtained commercially from ATCC, except the SW 1573 lines were obtained from Dr. H. Joenje, Free University, Amsterdam, Holland. All cell lines were maintained in liquid nitrogen storage until use. When in use for cytotoxicity testing, cells were maintained in exponential growth in plastic flasks (Falcon) in RPM1-164) medium containing 10% fetal bovine serum. All cell culture media and reagents were obatined from JRH or GIBCO.

Other chemicals were from Sigma. Cell lines grew as adherent monolayers. The adherent cultures were passaged to new flaks and fresh medium after brief (Leyva, 1990) trypsinization. SW 1573-21R60 is a variant subline of SW 1573 that is known to overexpress mdr-1 gene coding for P-glycoprotein -170 , thus representing classical multi-drug resistance (MDR). This MDR cell line is over 100 times less sensitive to the anti-cancer drugs, doxorubicin, vincristine, and etoposide, when compared to the parent cell line SW 1573.

Two normal human skin fibroblsts were used and maintained as with the tumor cell lines, except alpha-MEM medium was used for maintenance culture. CMH-F1 fibroblasts were originated in our laboarrory and CCD 973 fibroblasts was obtained from ATCC.

Cytotoxicity assay

Cytotoxicity was determined by the MTT assay in multi-well plates (Pieters, 1988; Leyva, 1990). Cells were plated in 96-well microplates in RMPMI-1640 medium plus 10% fetal bovine serum supplement with antibiotics (penicillin, streptomycin, fungizone; not toxic to human cells.) The number of cells plated varied for the different lines; in most cases 700-2000 cells per 100 μl per well. Plated cells were then allowed to equilibrate overnight. Plant extracts were diluted in culture medium and 100μl added to cells. The highest concentration of plant extract tested was always 5% that resulted in an ethanol concentration of about 1%. Ethanol was tested alone and found to be 30% growth inhibitory at 1%, and not inhibitory at 0.5%. Plant extracts were usually tested at several 2-fold serial dilutions. After cells were incubated with and without added test substances for 3 days under standard culture conditions, the number of metabolically viable cells was determined by the MTT tetrazolium dye assay.

Briefly, the old medium was removed. 200μl of fresh medium with 0.5mg/ml MTT was added. Cells were then further incubated for 3hr. The medium was removed and the blue black MTT formazan produced by metabolically active cells was dissolved with 150 μl of dimethyl sulfoxide. Absorbance was determined at 550nm using an ELISA plate reader (Cambridge Instruments). Absorbance was plotted versus plant extract concentration (%, vol/vol) to obtain dose-response curves. Cytotoxocity was measured as the IC_{50}, the concentration of plant extract or test agent that produces 50% decrease in the number viable cells (MTT absorbance) compared to untreated controls.

Fresh tumor specimens

Single-cell suspensions of tumor cells were obtained from surgical specimens of patients with cancer and examined for sensitivity to test substances, as reported by Leyva (1993) . Briefly, tissue was minced and then dissociated (i.e., broken apart) enzymatically and mechanically. Viable tumor cells were plated at 50,000/well in 96-well plates. Otherwise, the cytotoxicity assay was the same as for cell lines. An alternative method for small numbers of tumor cells to plate 5,000 cells in 6 -well plate in 1 ml 0.3% agar medium (semi-solid) with and without test agent. After 3 days incubation, MTT is added for overnight to stain viable cells.

The key to the labelled extracts in the following examples are as follows:

Labels	Plant
A	Centaurea
B	Capsicum
C	Sambucus
D	Lobelia
E	Myrrh
F	Echinacea
G	Goldenseal
H	Myrtle

EXAMPLE 1

All plant extracts were tested on HCT 8 colon tumor cells. All extracts evidenced some measure of anti-cancer activity with Myrrh and Centauraea exhibiting the most potent activity (see Figure 1).

EXAMPLE 2

Figure 2 summarizes data from 2-3 experiments for four different cell lines including HCT8, U138, U87 and CMH-F1 fibroblasts tested for sensitivity to the various plant extracts. Note that the plant extract exhibited relatively low toxicity to the normal cell line compared to the other cell lines tested.

EXAMPLE 3

All plant extracts were tested in at least HCT 8 tumor cells and normal fibroblasts. Plant extracts E.F and G were also tested in all 4 cell lines including U138 and U87 gliomas. Plant extract G was much less toxic to CMH-F1 fibroblasts and U138 glioma. In other recent experimental chemotherapy studies, it was found that U138 glioma cells are highly resistant to the plant derived anticancer etoposide. Similar results were seen for plant extracts E and F. Although plant extract A was moderately cytotoxic to HCT 8, it was exceptionally inactive against fibroblasts. Further experiments were conducted with plant extracts A.F, G and H in 2 fibroblast cell lines.

Figure 3 shows representative data for the two fibroblast lines; low sensitivities were observed for plant extracts A, F, G, and H,. Plant extracts G and H were the most cytotoxic at IC_{50}'s of 0.6 to 0.9%. Plant extracts A and F were several fold less active.

EXAMPLE 4

Plant extracts A-H were tested for cytotoxicity in SW 1573 and SW1573-2R160 to deterrmine if the cytotoxic substances in these plant extracts are similar to those natural plant drugs to which MDR tumor cells (2R160) are resistant. SW 1573 cells had a sensitivity profile for the different plant extracts similar to that of other tumor cells (Figure 4.) Plant extracts G and H were the most active at an IC_{50} of 0.4%. The least active were plant extracts B and D at an IC_{50} of 30%.

EXAMPLE 5

2R160 cells were less sensitive to the different plant extracts with IC_{50} values 2-3 times higher (Fig 5). Clearly, there was no evidence of drug resistance to the different plant extracts to the degree found for those natural product drugs including antibiotics, vinca alkaloids, epipodophyllotoxins, and taxol. The plant extract substances tested do not appear to be subject to explusion from cells by the transmembrane efflux pump (mdr-1 gene product).

EXAMPLE 6

Figure 6 shows the cytotoxic effects of plant extracts in primary cultures of two ovarian tumors (93-64 and 94-19) and one brain tumor (94-25).

EXAMPLE 7

Cytotoxic effects were studied with regard to cell survival (absorbance) expressed as % of control. Plant extract G was cytotoxic at IC_{50} of 0.5 to 1.2 % plant extract, levels similar to those observed for tumor cell lines. Plant extracts A, F and H were not active at concentrations as high as 5% plant extract, in most cases. Plant extract H did have modest activity against the brain tumor.

While the ovarian tumors did show sensitivity to conventional anticancer drugs (doxorubicin, cisplatin, cyclophosphamide), the brain tumor appeared to be multi-drug resistant.

EXAMPLE 8

In studies on A, G and H plant extracts it was found that their cytotoxic activities are not reversed by the presence of nucleosides and thus do not involve the syntheses of purine or pyrimidine precursors of RNA or DNA. Also, extract A, but not G or H, was more potent in cells with depletion of glutathione, a major detoxifying agent in all cells.

EXAMPLE 9

In a study of G and H it was demonstrated that both caused DNA damage as determined by a fluorescence procedure reported by Kanter and Schwartz (Mol. Pharmacol., 22:145-151, 1982). The effects were dose dependent after a 24-hour exposure period. Positive control used in these assays was etoposide. This can account for the cytotoxic as well cytostatic effect on tumor cells *in vitro*.

EXAMPLE 10

Finally, plant extract G has beem fractionated by a C18 reverse phase column using a 20% to 80% methanol linear gradient (over 40 minutes). Four fraction were observed with cytotoxic activity (as determined against colon tumor cells). Three of these fractions were stable and were further tested against 3 different cell lines.

Differential cytotoxicity was similar in fractions labeled X and Y, whereas fraction z was equally toxic to all 3 cell lines.

EXAMPLE 11

Fractionation of the individual extracts of A to H and further study of the individual fraction has demonstrated that these fraction were not the known cytotoxic agents such as Berberine, hydrastin, and Canadine.

EXAMPLE 12

A limited clinical study of the extract of all eight plants in 30 patients (whose cancers did not respond to standard treatment such as chemotherapy, radiotherapy and the like) gave remissions in 8 patients (partial response). Three of those 8 had a complete remission (2-3 year period) and were not using any other form of therapy at the time of remission.

EXAMPLE 13

A brief clinical was conducted on 4 patients studied before and after 2 weeks and 1 month, respectively, of post use of the extract of all eight plants (same as example 12, above). The patients received two teapoons of the extract daily (one teaspoon twice daily or ½ teaspoon four times daily). The patients exhibited no adverse clinical effects and no change in CBC and no change in body chemistries. The following laboratory changes were observed using flow cytometry techniques using monoclonal antibodies for the respective markers as set forth below. The analysis indicated the following changes:

- Increase in CD3/CD16+56 NK cells in 4/4 pateints;
- Increase in CD8/CD57 NK cells in 2/4 patients. In 1 pt very high baseline levels. Pt Was taking supplement on/off before testing;
- Decrease in CD 38 cells in 1/4 patients;
- Increase in CD 38 cells in 1/4 pateints;
- Increase in CD 19/25-borderline in 1/4 patients.

In sum, the results indicated evidence of a heightened number of NK cells (heightened immune response) which could explain, at least in part, the anticancer activity which is associated with the presnt compositions.

It is to be understood by those skilled in the art that the foregoing description and examples are illustrative of practicing the present invention, but are in no way limiting. Variations of the detail presented herein may be made without departing from the spirit and scope of the present invention as defined by the following claims.

CLAIMS

1. A method of treating cancer in a patient in need of cancer therapy comprising administering to said patient by ingestion or by topical application an anti-cancer effective amount of a composition comprising an extraction product of at least two plants selected from the group consisting of centaurea, capsicum, sambucus, lobelia, myrrh, echenicia, goldenseal and myrtle.

2. A method in accordance with claim 1, wherein the plants comprise a binary mixture in a weight proportion ranging from 3:1 to 1:3.

3. A method in accordance with claim 1 wherein a three-way mixture initially comprises:

(a) 30% to 70% Goldenseal
(b) 20% to 40% Myrtle
(c) 5% to 20% Centaurea

4. A method in accordance with claims 1 or 3 wherein a three-way mixture initially comprises:

(a) 35% to 65% Goldenseal
(b) 25% to 35% Myrtle
(c) 7% to 15% Centaurea

5. A method in accordance with claim 1 wherein all eight plants are extracted and the said plants initially comprise the following percentages by weight

(a) 3% to 5% Centaurea
(b) 1.5% to 4% Capsicum
(c) 1.5% to 3% Sambucus
(d) 1.5% to 4% Lobelia

(e) 20% to 40% Myrrh

(f) 30% to 50% Echinacia

(g) 15% to 25% Goldenseal

(h) 3% to 5% Myrtle

optionally, (i) 2% to 5% Burdock and/or

(ii) 0.5% to 1% by weight Saffron.

6. A method in accordance with claim 1 wherein all eight plants are extracted and said plants initially comprise the following percentages (by weight).

(a) 2% to 4% Centaurea

(b) 2% to 3% Capsicum

(c) 2 % to 3% Sambucus

(d) 2% to 3% Lobelia

(e) 25% to 35% Myrrh

(f) 35% to 45% Echinacia

(g) 18% to 22% Goldenseal

(h) 35% to 4.5% Myrtle

7. A method in accordance with any of Claims 1 to 6 wherein the mixture is extracted with a solvent chosen from the group consisting of water, ethyl alcohol, and mixtures, thereof.

8. A method in accordance with any of Claims 1 to 7 wherein the mixture is extracted with water.

9. A method in accordance with any of Claims 1 to 7 wherein the mixture is used as a tincture, solution or powder.

10. A method in accordance with any of Claims 7 to 9 wherein the mixture is used as a

tincture.

11. A method in accordance with any of Claims 9 to 10 wherein the tincture contains 10% to 45% ethyl alcohol by volume.

12. A pharmaceutical composition useful against cancer in mammals containing as active ingredient a composition prepared by extracting one or more plants selected from the group consisiting of centaurea, capsicum, sambricus, lobelia, myrrh, echenicia, goldenseal and myrtle.

13. A composition in accordance with Claim 12 wherein the plants in a binary mixture are initially present in the proportion of 3:1 to 1:3.

14. A composition in accordance with Claim 12 wherein a mixture initially comprises:

(a) 30% to 70% Goldenseal
(b) 20% to 40% Myrtle
(c) 5% to 20% Centaurea

15. A composition in accordance with Claims 12 and 14 wherein a mixture initially comprises:

(a) 35% to 65% Goldenseal
(b) 25% to 35% Myrtle; and
(c) 7% to 15% Centaurea

16. A composition in accordance with Claim 12 wherein all eight plants are extracted and the said plants initially comprise the following percentages by weight:

(a) 3% to 5% Centaurea

(b) 1.5% to 4% Capsicum

(c) 1.5% to 3% Sambucus

(d) 1.5% to 4% Lobelia

(e) 20% to 40% Myrrh

(f) 30% to 50% Echinacea

(g) 15% to 25% Goldenseal

(h) 3 % to 5% Myrtle

optionally, (i) 2% to 5% Burdock and/or

(ii) 0.5% to 1% by weight Saffron.

17. A composition in accordance with Claim 12 wherein all eight plants are extracted and said plants initially comprise the following percentages (by weight).

(a) 2% to 4% Centaurea

(b) 2% to 3% Capsicum

(c) 2% to 3% Sambucus

(d) 2% to 3% Lobelia

(e) 25% to 35% Myrrh

(f) 35% to 45% Echinacia

(g) 18% to 22% Goldenseal

(h) 3.5% to 4.5% Myrtle

18. A composition in accordance with any of Claims 12-17 wherein the mixture is extracted with a solvent chosen from the group consisting of water, ethyl alcohol, and mixtures thereof.

19. A composition in accordance with any of Claims 12 or 17 wherein the mixture is extracted with water.

20. A composition in accordance with any of Claims 12 to 19 wherein the mixture is

used as a tincture.

21. A composition in accordance with any of Claims 12 to 20 wherein the mixture is used as a tincture, solution or powder.

22. A composition in accordance with any of Claims 12 to 21 wherein the tincture contains 10% to 45% ethyl alcohol by volume.

23. A composition prepared by extracting a mixture of two or more plants selected from the group consiisting of goldenseal, myrtle, and centaurea wherein the binary mixtures are in the proportions of 3:1 to 1:3 and the three-way mixture consists of:

(a) 30% to 70% Goldenseal
(b) 20% to 40% Myrtle
(c) 5% to 20% Centaurea

24. A composition in accordance with Claim 23 wherein the mixture is extracted with a solvent chosen from the group consisting of water, ethyl alcohol, and mixtures, thereof.

25. A composition in accordance with Claims 23 or 24 wherein the mixture is extracted with water.

26. A method of treating cancer comprising administering to a patient in need thereof an anti-cancer effective amount of a composition comprising at least two extracts of plants selected from the group consisting of Centaurea, Capsicum, Lobelia, Myrrh, Echinacea, Goldenseal and Myrtle.

27. The method in accordance with claim 26 wherein said two extracts are present in a ratio of 3:1 to 1:3.

28. The method according to claim 26 wherein said composition contains at least three of said plant extracts.

29. The method according to claim 26 wherein said composition comprises:

a) 30% to 70% by weight of Goldenseal extract;
b) 20% to 40% by weight of Myrtle extract; and
c) 5% to 20% by weight of Centaurea extract.

30. The method in according with claim 29 wherein said composition comprises:
a) 35% to 65% by weight Goldenseal extract;
b) 25% to 35% by weight Myrtle extract; and
c) 7% to 15% by weight Centaurea extract.

31. The method according to any of claims 26-30 wherein said extracts are substantially free of berberine, hydrastin and canadine.

32. The method according to any of claim 26, 28 or 31 wherein said composition comprises extracts of all seven of said plants.

33. A method according to claim 32 wherein said composition consists essentially of :

a) 3% to 5% by weight Cantaurea extract;
b) 1.5% to 4% by weight Capsicum extract;
c) 1.5% to 4% by weight Lobelia extract;
d) 20% to 40% by weight Myrrh extract;
e) 30% to 50% by weight Echinacea extract;
f) 15% to 25% by weight Goldenseal extract; and
g) 3% to 5% by weight Myrtle extract.
optionally, (i) 2% to 5% Burdock and/or

(ii) 0.5% to 1% by weight Saffron.

34. A method according to claim 33 wherein said composition consists essentially of :

a) 2% to 5% by weight Cantaurea extract;
b) 2% to 3% by weight Capsicum extract;
c) 2% to 3% by weight Lobelia extract;
d) 25% to 35% by weight Myrrh extract;
e) 35% to 45% by weight Echinacea extract;
f) 18% to 22% by weight Goldenseal extract; and
g) 2.5% to 4.5% by weight Myrtle extract.

35. A method according to claim 26 wherein each of said extract is obtained by:

-mixing the plant with a solvent selected from the group consisting of water, ethyl alcohol and a mixture of water and ethyl alcohol;

-bringing the mixture of said liquid phase and said solid phase to a temperature of at last 70°C;

-optionally adding to the liquid phase at a temperature less than the boiling point of ethyl alcohol an amount of alcohol sufficient to provide a concentration of 10% to 30% ethyl alcohol by volume;

-permitting the mixture to stand for at least about two weeks;

-filtering to obtain the liquid phase which constitutes said extract; and

-optionally removing alcohol or water from said liquid phase or adding additional alcohol or water to said liquid phase.

36. The method according to claim 35 wherein said solvent is water.

37. The method according to claim 35 wherein said solvent is a mixture of water and ethyl alcohol.

38. The method according to claim 38 wherein said composition is a liquid further comprising water, ethyl alcohol or a mixture of water and ethyl alcohol.

39. A method according to claim 38 wherein said composition is administered in a dosage of 10 to 40 drops, 4 to 6 times per.

40. A method according to claim 26 wherein said composition is administered in a dosage ranging from 1 to two teapsoons a day.

41. A process for extracting an anti-cancer composition from two or more plants selected from the group consisting of Centaurea, Capsicum, Lobelia, Myrrh, Echinacea, Goldenseal and Myrtle, comprising:

-mixing one or more of said plant with a solvent selected from the group consisting of water, ethyl alcohol and a mixture of water and ethyl alcohol to provide a liquid phase and a solid phase;

-bringing the mixture of said liquid phase and said solid phase to a boil;

-cooling the mixture and optionally adding an amount of ethyl alcohol to the liquid phase sufficient to provide a concentration of 10% to 30% ethyl alcohol by volume;

-permitting the mixture to stand for at least about two weeks;

-filtering to obtain the liquid phase which constitutes said composition;

-mixing the resulting extracts, if applicable; and

-optionally removing alcohol or water from said liquid phase or adding additional alcohol or water to said liquid phase.

42. The process for preparing an anti-cancer compostion, comprising extracting at least three of said plants according to the process of claim 41, and mixing the resulting extracts, if applicable.

43. A pharmaceutical composition obtained by the process of claim 41 or 42.

FIG. 1

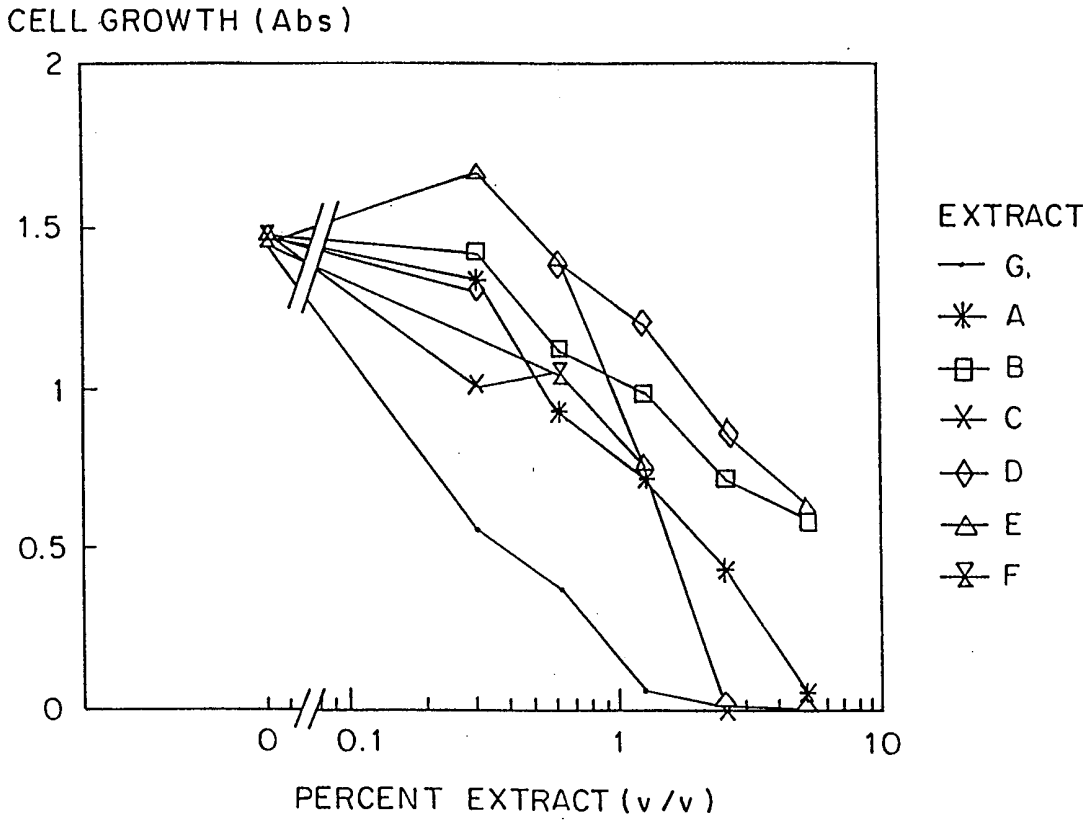
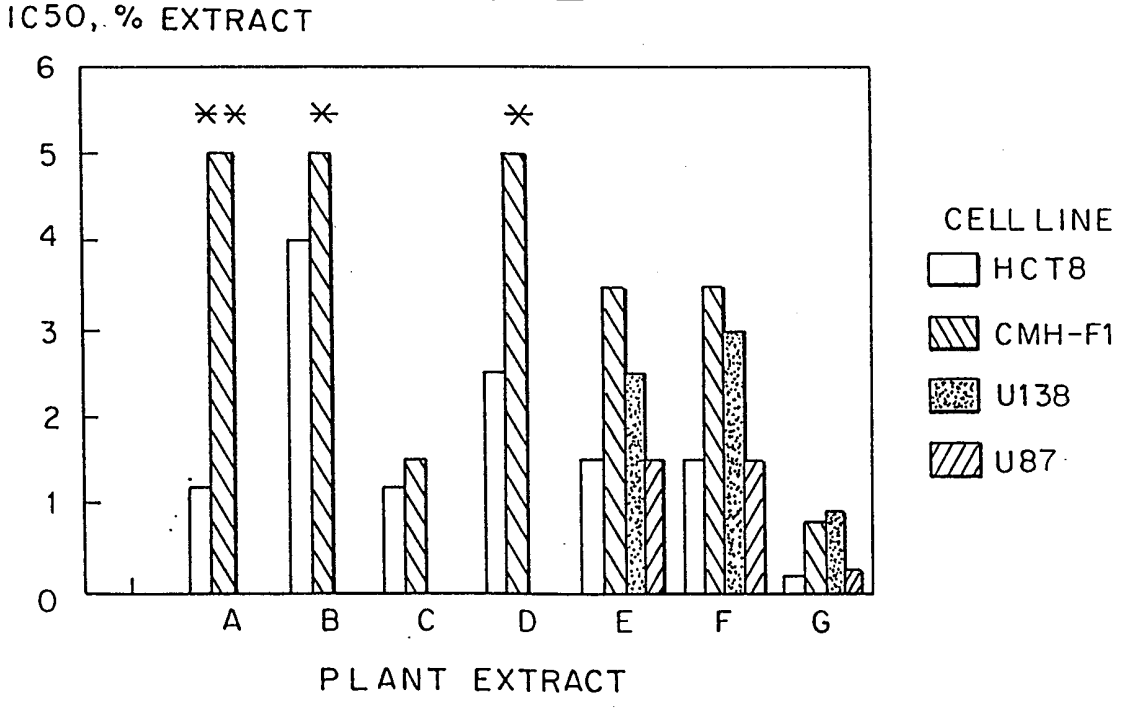


FIG. 2



* > 5 % ** >> 5 %
(LOWER THE IC50, HIGHER THE POTENCY)

FIG. 3

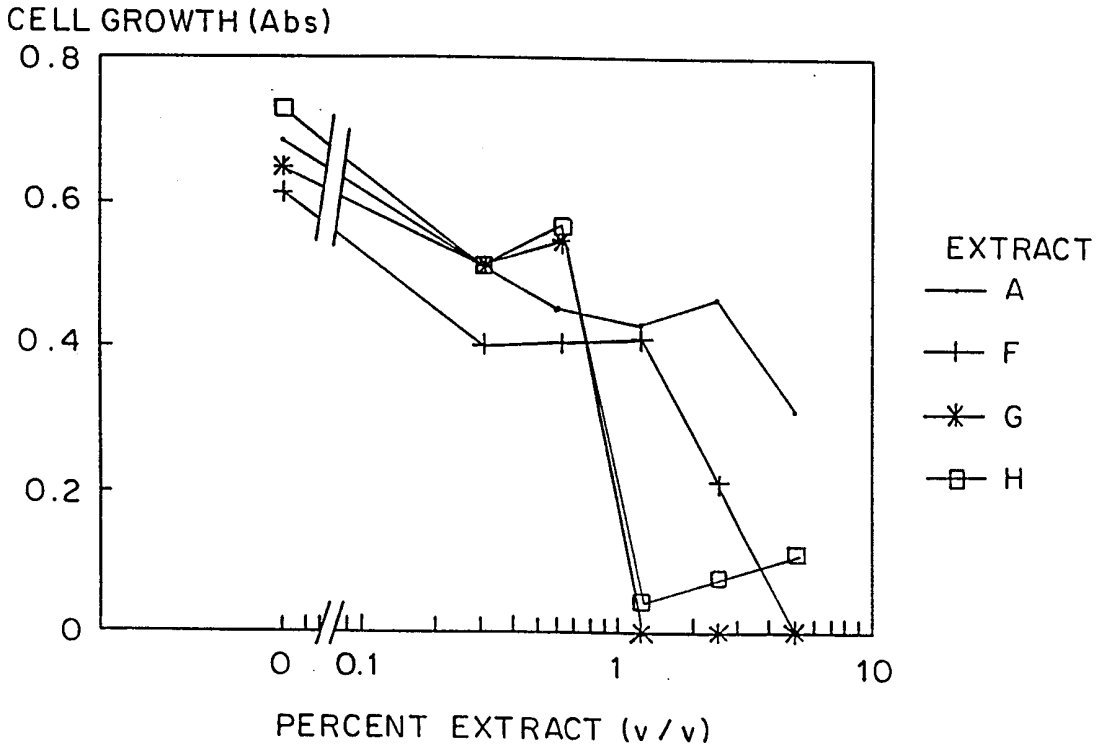

CELL GROWTH (Abs)
0.8
0.6
0.4
0.2
0
0
0.1
1
10
PERCENT EXTRACT (v / v)
EXTRACT
A
F
G
H

FIG. 4

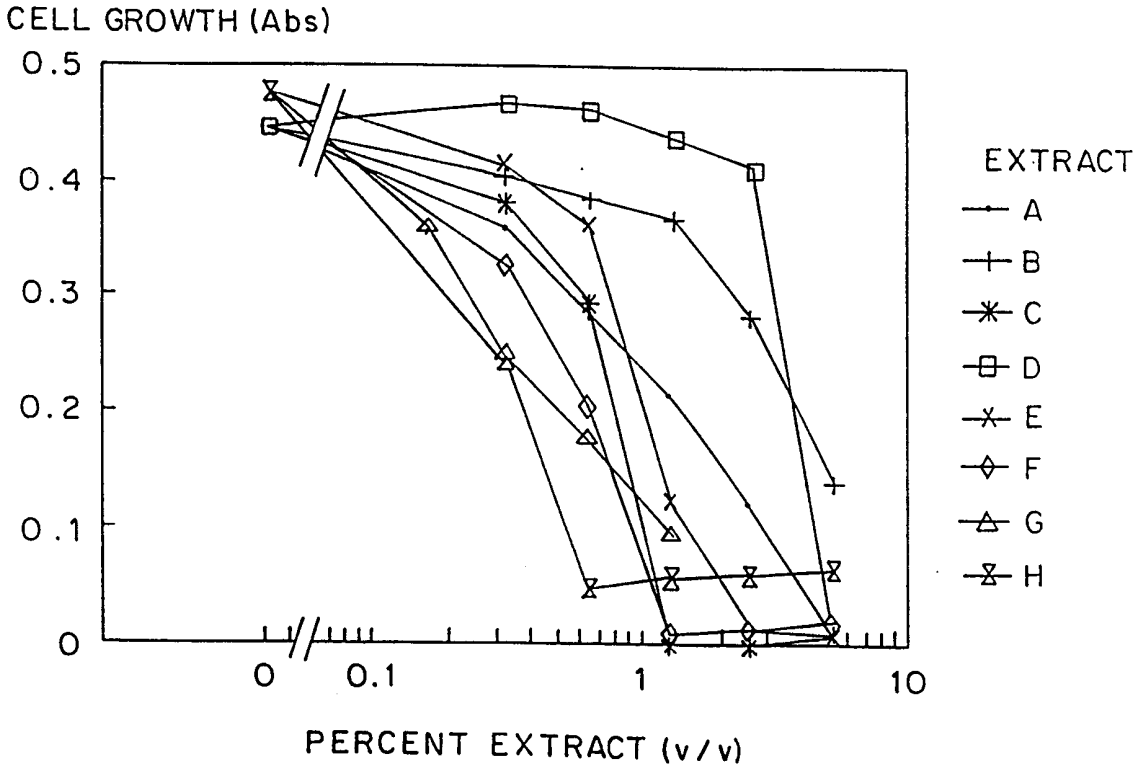

CELL GROWTH (Abs)
0.5
0.4
0.3
0.2
0.1
0
0
0.1
1
10
PERCENT EXTRACT (v / v)
EXTRACT
A
B
C
D
E
F
G
H

FIG. 5

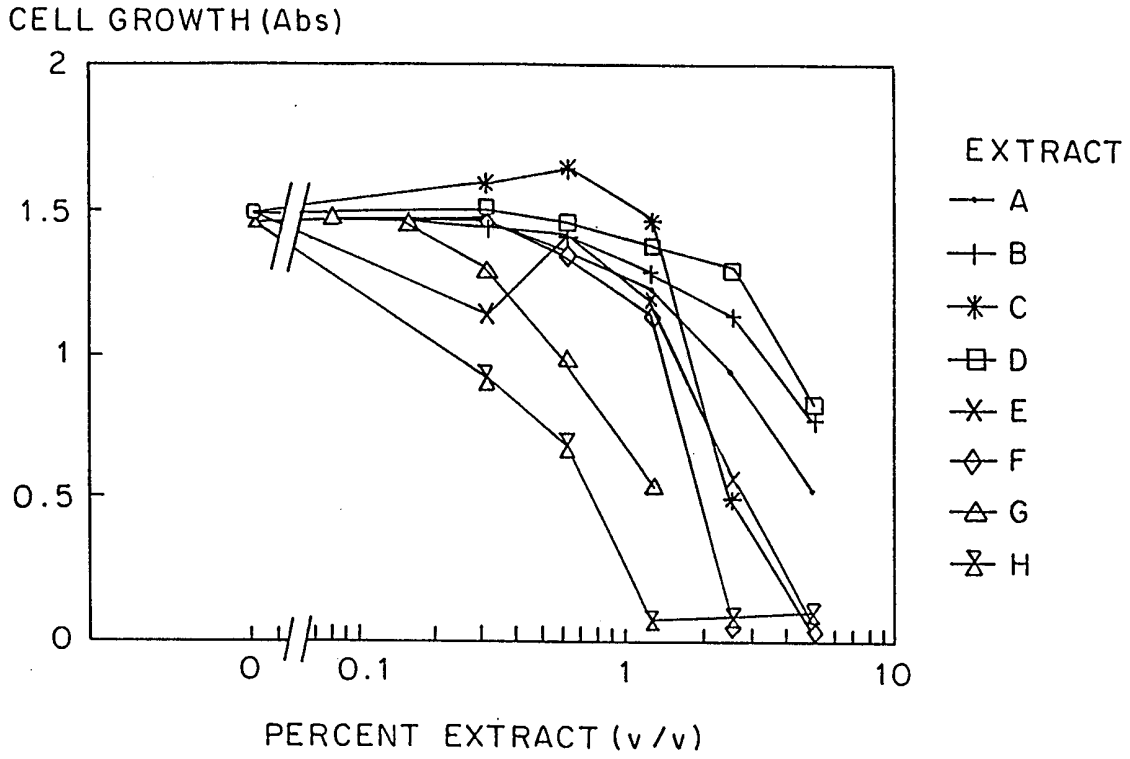
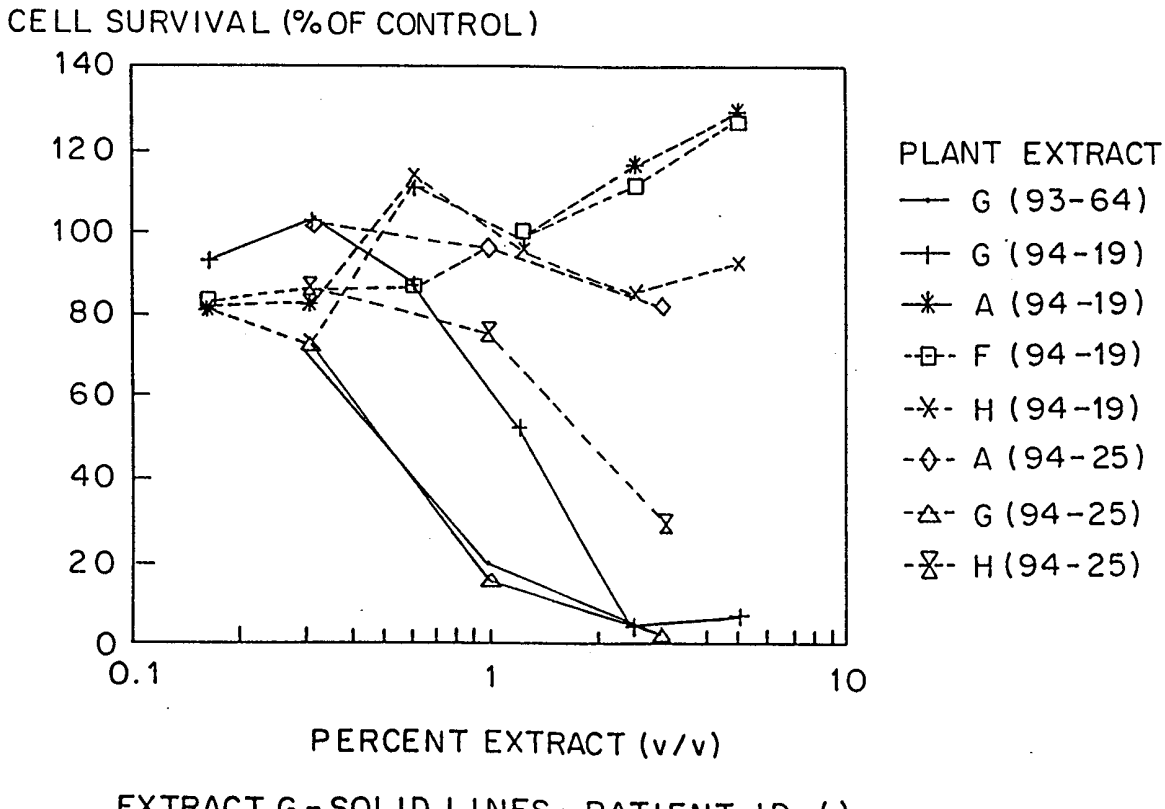


FIG. 6



EXTRACT G - SOLID LINES; PATIENT ID - ( )

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04109

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 35/78
US CL :424/195.1; 426/531, 655

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/195.1; 426/531, 655

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS including USPAT, JPO, and EPO

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	US 3,932,628 A (HUDSON) 13 January 1976, col. 3, Table II, and claims 1 and 8.	12 --- 1, 2, 13, 26-28, 31, 41-43
X - Y	US 5,714,163 A (FORSSEN et al) 03 February 1998, col. 1, lines 17-31.	12 --- 1, 2, 13, 26-28, 31, 41-43
X - Y	US 5,804,168 A (MURAD) 08 September 1998, col. 2, lines 31-51.	12 --- 1, 2, 13, 26-28, 31, 41-43

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
11 MAY 1999

Date of mailing of the international search report
28 MAY 1999

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04109

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	JP 7101868 A (KODOMA et al) 18 April 1995, see abstract.	12 --- 1, 2, 13, 26-28, 31, 41-43
X - Y	JP 8055427 A (HIRAMATSU et al) 01 April 1983, see abstract.	12 --- 1, 2, 13, 26-28, 31, 41-43
X - Y	WO 9813053 A1 (RUEPP, M.) 02 April 1998, see abstract.	12 --- 1, 2, 13, 26-28, 31, 41-43
X --- Y	WO 9420540 A1 (GIRBES et al) 15 September 1994, see abstract.	12 --- 1, 2, 13, 26-28, 31, 41-43

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04109

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 7-11, 18-22, 32-34
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.