

Plant Products with Anti-cancer Properties Employed in the Treatment of Bowel Cancer: Literature Review 1985 and 2004

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ABSTRACT

The use of extracts of plant origin for the treatment of cancer has seen renewed interest. In Mexico, "Herbalists" have practiced since before Spanish times, but now at Mexican medical schools the alternative medicines are not taught. The aim of this work was to carry out a review of the international literature to identify and analyze the use of articles in the treatment of cancer with principles of plant origin. An online review was conducted of citations published between 1985 and 2004, selecting those works in which plant products demonstrated pharmacological activity useful against cancer with particular reference to bowel carcinoma. In 45 articles, we looked for common and scientific names, part of plant and/or its products used as treatment or preventive, used in an experimental *in vivo* or *in vitro* model, pharmacological effects and actions, human or animal species studied and apparent efficacy. Fifty-five percent used human cancer cell lines as a model, incubated with plant extracts; 40% used animal species to induce tumors and protect them with plant extracts; only 5% were clinical studies. Additionally, we determined which of these natural products are included in relevant references: two are marketed in Mexico; none were listed in the academic Mexican book "Vademecum Ademico de Mdicamentos;" one was found in Goodman Gilman's The Pharmacologic Basis of Therapeutics, while three were listed in Katzung's Medical Pharmacology. Experimental data support the empirical use of natural plant products against cancer by their chemopreventive effects, but they are not considered drugs. Despite not being listed as drugs, these remedies should be covered in pharmacology courses when evidence of mechanisms of action is available. Our review suggests that medical schools should review "traditional medicines" in order that graduates know what treatments patients are using and those that may be of value.

INTRODUCTION

The use of plant products in the treatment of cancer has been of recent interest [46]. In the market these

products are offered as "natural products" [47]. The development of natural products used as medicines represents a way to rescue valuable aspects of traditional culture. In Mexico the "Herbalist" has been practicing before Spanish times [48]. Despite their unproven safety, in Mexico some plant products are used as drugs but are registered with the Secretary of Health as food, or food supplements, and they are sold without prescription. Though they are used widely, in Mexican schools the pharmacology of these alternative medicines is not taught unless by independent study [49]. In the scientific literature numerous citations reference epidemiological studies that support significant differences in the occurrence of carcinoma between oriental and occidental populations [33,40]. Populations with a high level of natural herbal product use have a reduced incidence of gastric cancer [29,50], as exemplified by the low incidence of colon cancer in Asian countries with a high consumption of soybean products [17]. Soybeans are the major dietary source of saponins, which have been suggested as possible anticarcinogens [26]. Increased consumption of vegetables reduces the risk of colorectal cancer mortality [38]. For this reason, there is a great interest in screening plants used in traditional medicine in Africa, Panama and Mauritius for chemotherapeutic activity [35]. Cancer is a very important national health problem in Mexico [13] and the use of traditional plant products as chemopreventative or chemotherapeutic treatments requires further study. The aim of this work was to carry out a review of the international literature to identify and analyze the articles that mentioned anticancer biological activity of principles from plant origin, in particular bowel carcinoma. Additionally we determined which of these natural products mentioned in the international literature are included in the commercial and academic information employed in Mexican marketing and in medical schools.

MATERIAL AND METHODS

A review of the international medical literature online was made over a period of 20 years (1985-2004), selecting those works in which authors reported the use of plant products with some pharmacological activity useful as a treatment against cancer, in

particular, for bowel carcinoma. Additionally we reviewed the PLM book at commercial marketing ("Pharmaceutical Specialties Dictionary" [47]) and tree academic books, one national (*Vademecum Academico de Medicamentos* [51]) and two

Minternational (Goodman Gillman's "The Pharmacological Basis of Therapeutics" [52] and Katzung B., "Farmacología Básica y Clínica" [50]).

Table I. Analyses of the literature reviewed between 1985 and 2004 that references the use of natural products as therapeutics for the treatment of prevention of cancer.

Common and scientific name; preparation	Active principle	Human	Chemoprotective effect	T	P	Animal and CA method	V	v	Actions	Country, City. First author, year	
Mistletoe <i>ABNOB</i> <i>Aviscum mali</i> extract:	Mistletoe lectin 1 PATIENTS 3-24 weeks	Sera patients with tumors	immunomodulatory	+				+	+	Activate B-cells to develop specific antibodies to chitin- binding mistletoe lectin 1	Germany, Tubingen. 1. Klein R, 2004
Ginko <i>Ginko biloba</i> , Extract of leaves	Extract in diet/day 50- 500 ppm or Bilobalide 15-500 ppm; 4 weeks		Antiproliferative (Significant ↓ in ACF in colon)		+	F-344 male rat; 2 weeks ¹		+	+	↓ Nuclear antigen on proliferating cells. CP450: ↑Glutathione S-transferase and quinine reductase	Japan, Ishikawa. 2. Suzuki R, 2004
Soy Glycine max Crude Soy saponin extract	Crude Soy saponin extract by 72 h: ↓ Cell growth dose- time related 1, 2, 3d	Adenocarcinoma cells line (HT-29) from colon	Antiproliferative: ↓ tumorigenesis by antiinflammatory activity			HT-29 ²			+	Supress degradation of Ikappa Balpha in PMA- stimulated cells. Down regulated: PCK, COX2	South Korea, Seoul. 3. Kim HY, 2004
<i>Daphne genkwa</i> (Thymelaeaceae) and Jyu-So-To	Organic extract of Daphne and medical prescription of Jyu- So-To 236ppm/ water/day		Antitumor, antiinflammatory and antiallergy		+	Mice ^{1,3,4}		+	+	Jyu-So-to reduce ¹ 46.7% <i>D. genkwa</i> : reduce ³ (n-hexane 30.8%; methanol extracts 56.3%); water extract inhibited ⁴	Japan, Tokyo. 4. Kai H, 2004
Cranberry <i>Vacciniummacrocarpon</i> <i>Ait.</i> Extract & phyto- chemicals (flavonol glycosides, antho- cyanins, proantho- cyanidins organic & phenols ac.	Polyphenol fraction is more active than Total Cranberry Extract (TCE) 200 µ/ml	Cancer cell lines ⁶ (oral, colon, prostate)	Antiproliferative activity could be enhanced by total polyphenols plus TCE		+	9 cancer cell lines ⁶			+	Antiproliferative vs CA: Oral 96% vs KB, 95% vs CAL27; colon 92% vs HCT116, 61% vs HT-29, 60% vs SW480, 63% vs SW620; prostate 95% vs RWPE-1, 95% vs RWPE-2, 99% vs 22Rv1.	USA, California. 5. Seeram NP, 2004
Black Shokeberry <i>Aronia meloncarpa E</i> Anthocyanin extract from fruits	50 mg/ml/24 h (monomeric anthocyanin) ¿specific suppressor component?	Normal colon (NCM460) and Colon cancer cell lines (HT-29)	Cytostatic inhibition of cell growth (antioxidant used as food coloring agent).		+	NCM460 And HT- 29)			+	60% inhibition HT-29 (Blockage G1/G0 and G2/M phases of cell cycle); 35% ↓ in COX2 gene expression in HT29	USA, Maryland. 6. Malik M, 2003
St. Jhon's Wort <i>Hypericum amblycalyx</i> Petroleum ether extract aerial parts	Acylphloroglucinol derivatives: Hypercalyxone A and B and two semi synthetic compounds	Cancer cells KB and Jurkat T	Cytotoxic and antibacterial		+	KB and Jurkat T Cancer cells			+	All has moderated cytotoxic activity vs KB and Jurkat T. Compounds 3 and 4 antibacterial strong activity vs Gram +	Switzerland, Zurich. 7. Winkel- mann K, 2003
Bamboo <i>Bamboo</i> Porphyrin photo sensitizer from leaves: methanol extract	201- dihydroxypurpurin-7 delta-lactone ethyl methyl diester and the corresponding methyl phythyl diester, its activity were enhanced by brief irradiation with fluorescent lamp	Leukemia and colon adenocarcinoma	Apoptosis in cancer cell lines enhanced by photodynamic induction with fluorescent lamp		+	CMK-7 And Colo320 DM			+	Apoptosis leukemia CMK7; colo320 DM. Promising photo sensitizers for dynamic therapy of CA	Korea, Kyungnam. 8. Kim KK, 2003
Puyang <i>Zingiber aromaticum</i> Extract rhizomes and	Zerumbone (2,6,9 humulatriene-8-one, a sesquiterpenoid) IC50 10 mM Vs curcumin from <i>Curcuma longa</i> (IC50, 25 mM).	Cancer cell lines	Anticancer activity, concentration- dependent increase in apoptosis antiproliferative.		+	1 Rat fed extracts. HT-29, CaCo-2 and MCF-7 ^{1,7}		+	+	Apoptosis HT-29 (cycle arrest in G0/G1 and G2/M, CaCo-2 and MCF-7. In rats aberrant crypt foci (ACF) were reduced	Australia, Adelaide. 9. Kirana C, 2003
Sapodilla <i>Manikara zapota cv.</i> Tikal. Methanol extract fruit	Methyl 4-O-galloyl- chlorogenato (1) and 4-O-galloyl- chlorogenic acid (2) (+ 8 polyphenolic antioxidants)	Colon cancer cell lines	Antioxidants ⁵ (IC50: 12.9 y 24 µM, for 1 and 2, respectively)			HCT- 116, SW480			+	Cytotoxicity vs Colon Ca HCT- 116, SW480: IC50, 190-160 y 154-134 µM, respectively	USA, New York. 10. Ma J, 2003
Nirgundi <i>Vitex negundo</i> Chloroform extract leaves	Flavones analogues of vitexicarpin and 3,5'dihexanoyloxy- 3,6,7,4'-tetrametho- xyflavone (9)	Cancer cell line panel	Cytotoxicity		+	Lu1, KB and LNCaP. Mouse			+	Vitexicarpin and its analogue are cytotoxic <i>in vitro</i> <i>In vivo</i> : (9) Analogue is inactive in hollow fiber assay with Lu1, KB and LNCaP at highest dose 40 mg/kg; and P-388 Leu. Model with 135 mg/kg	USA, Chicago. 11. Diaz F, 2003

Table I. Continued

Common and scientific name; preparation	Active principle	Human	Chemoprotective effect	T	P	Animal and CA method	V	v	Actions	Country, City, First author, year
Mistel <i>Viscum album</i> aqueous extract (BIOTHERAPY)	Isorel	Cervical CA HeLa cells; Colorectal CA Dukes C o D: Prospective, randomized, controlled: CX, surgery +5FU 6 cycles or Idem+isorel ¿dose?	Anticancer <i>in vivo</i> , <i>in vitro</i> : CA colon HT29	+		murine melano- ma B16F10. HT29 ⁷ .	+	+	Improve patients' resistance; render side effect more tolerable: > X survival > cumulative proportion survival (Kaplan-maier) Cx+Chemotherapy + Biotherapy	Romania. 12. Cazacu M, 2003
Saffron <i>Crocus sativus</i> L. dried red-dark stigmas, crude extract	Carotenoids: 12 components isolated by HPLC with photodiode-array detection	malignant cells <i>in vitro</i>	CHEMOPREVENTI VE (use agents to prevent or block the development of CA). Suggestion: use in clinical trials		+	Colony forma- tion assay. Ames m.	+	+	Cytotoxic vs HeLa cells Saffron is not toxic, non- mutagenic, non-antimutagenic and non-co mutagenic.	México, México. 13. Abdullaev J, 2002
Bilberry <i>Vaccinium myrtillus</i> . Ethanol extract	Delphinidin, malvidin (anthocyanins)	Colon carcinoma and Leukemia cells	Apoptosis; nucleosomal DNA fragmentation; Radical scavenging activity		+	HL60,		+	Apoptosis in HL60 leu > HCT116 colon CA. Malvidin no effect in HCT116 Nucleosomal DNA fragmentation was not induced in HCT116	Japan, Hiroshima 14. Katsube N, 2003
Sculap <i>Scutellaria baicalensis</i>	0.1-100 mg/ml/72 h	Cancer cell lines: Squamous, colon, breast, prostate, hepatocellular,	Anticancer Anti-inflammatory		+	Viable cells ¹³ PGE(2) productio n ¹⁴		+	Squamous cell SCC-25, KB; Breast MCF-7; hepatic HepG2; >Prostate PC-3, LNCaP; >colon KM-12, HCT-15. Dose dependent inhibition in all cell lines, >colon >pros	USA, NY. 15. Ye F, 2002
Wax tree <i>Rhus succedanea</i> ethanolic extract of the Sap	Heptadecatrien y decadienylhidroquino ne, heptadecenyl- hidroquinone	Cancer cell lines	Antioxidative and citotoxic					+	Activity against five cancer cell lines	Taiwan, Tainan. 16. Wu PL, 2002
Soybean <i>Glycine max</i> Extract soluble fraction	Proteins and soluble components 1-6%, vol/vol/24 h. Isoflavones genistein 12.5 µg/ml idem		Preventive Cell death		+	Cell death ¹⁵ Citologic al marker ¹⁶		+	Vacuoles, very flat, giants and cell death CaCo-2, SW620, HT- 29. Involved Golgi apparatus Anticancer reducing protein not avoid effect	USA, Chicago 17. Zhu Q, 2002
Mistletoe <i>Phoradendron brachystachyum</i> Aquous extract	Lectin 1(ML-1) Viscotoxins (VT)	Tumors: sera from patients treated with ABNOBavisum mali (AM) for 18 Weeks	Immunomodulator	+		ELISA vs viscotoxi ns		+	ML-1, VT activates B-cells and VT antibodies specific: antibodies IgG1, IgG3 vs ML-1 y VT (92% patients) X: 6-9 W No cross reactivity (independent)	Germany, Tubingen. 18. Klein R, 2002
Aster oharai Methanolic extract of aerial parts	5 new Labdane diterpenes:	Cultured human tumor cell lines	Cytotoxicity (anticancer)					+	Only one showed moderate cytotoxicity vs four cell lines ED50 1.1 to 7.7 mcg/ml	Korea, Suwon. 19. Choi SZ, 2002
Bollen <i>Kageneckia Oblonga</i> Extracts of global methanol (methanol, hexa- ne, dichlorome- thane)	Prunasin, 23,24- dihydro-cucurbitacin F, and a new cucurbitacin	Tumoral cell lines	Antipyretic, analge sic, antiinflammat ory, antioxidant: by both cucurbitacins and other					+	Non toxic vs human neutrophils Cytotoxicity vs p-388 murine leukemia, A-549 lung , HT-29 colon	Chile, Santiago. 20 Delporte C, 2002
Casearia <i>Casearia lucida</i> Metanolic extract of the bark from Madagascar	Clerodane diterpenoids namely casearucins A-K (11)	Cancer cell lines	Cytotoxicity		+			+	All showed cytotoxicity vs A2780 ovarian CA. But none of six clerodane diterpenes selected showed selectivity vs multiple cell lines	USA, Virginia. 21. Sai Prakash, 2002
Mahajo <i>Casearia silvestris</i> Metanolic extract of leaves and twigs from Madagascar	Clerodane diterpenoids (3) and casearvestrins A-C	Tumor cell lines	Cytotoxicity and antifungal			disk diffu- sion assay vs fugny		+	Against KB cell and Antifungal growth inhibition of <i>Aspergillus niger</i>	USA, North Caroline. 22. Oberlies NH, 2002
Indigo plant Salomon's seal <i>Polygonum tinctorium</i> <i>Lour</i> Extracts	ethylacetate- and tryptanthrin crude		Chemopreventive activity		+	F344 rats ¹		+	Reduce incidence of atypical cripts and Intestinal tumors	Japan, Okayama. 23. Koya Miyata, 2001
Ginger <i>Curcuma</i> spp Satndarized extract oral	Curcumin	Human blood after incubation with lipopolisacaride (LPS)	Chemopreventive by inhibition of COX- 2 activity implicated in human CA: its inhibition as biomarker		+	Preclini cal carcino- genic models		+	Reduce the LPS induced COX- 2-protein levels and PGE2	U. kingdom, Leicester. 24. Plummer SM, 2001

Table I. Continued

Common and scientific name; preparation	Active principle	Human	Chemoprotective effect	T	P	Animal and CA method	V	v	Actions	Country, City, First author, year
Apiacea <i>Steganotaenia araliacea</i> Organic extract	10-demethoxystegane Steganone, prestegane B.	Ovarian cancer cell line	Antiproliferative		+			+	Antiproliferative Vs ovarian CA cell (OVCAR-3)	USA, Maryland. 25. Meragelman, 2001
Soybean Glycine max > dietary source of saponins	saponins		Inhibing cell proliferation		+	HT-29 colon CA		+	Suppresses PKC activation and induces differentiation, which possibly mediate the growth inhibition of tumor cells.	Korea, Seoul 26. Oh Y.J. 2001
Wheat germ Fermented extract (2001)	Standarized to 2-6-dimethoxy-p-benzoquinone		Prevents colonic cancer			F344 Rats ¹	+		Reduced % animal developed tumor and number of tumors per animal, and the number of aberrant crypt foci	Hungary, Budapest; 27. Zalattai A, 2001
Nam ginseng <i>Dracaena angustifolia</i> Metanol extract of roots, rhizome	Nine spirostanol steroids(namogenins A-C), eighth steroidal saponins	Cancer cell lines	Anticarcinogenic comparable to doxorubicin		+			+	Antiproliferative vs murine colon 26-L5, human HT-1080 ribosarcoma, melanomaB-16 BL6	Japan, Toyama; 28. Tran QL 2001
Garlic <i>Allium sativum</i> Aqueous extract		Cancer cell lines	Anticarcinogenic		+			+	Arrest cell cycle at the G2/M boundary and differential gene expressionHT-29 cell	USA; 29. Frantz DJ, 2000
Garlic <i>Allium sativum</i> Freshly crushed	Allicina	Cancer cell lines	Anticarcinogenic		+			+	Antiproliferative of mammary MCF-7, endometrial (ishikawa) and colon HT-29; and fibroblast	Israel, Beer-Sheva; 30. Hirsch K, 2000
<i>Alpinia blepharocalyx</i> Etanol extract of seeds	Diarylheptanoids (11) y 2 derivatives	Cancer cell lines	Anticancerigenic					+	Citotoxicity vs Murine colon 26-L5; HT-1080 fibrosarcoma	Japan, Toyama; 31. Tezuka Y, 2001
Bittermelon <i>Momordica charantia</i> Linn. Ethanol extract	0.5, 1.0, 1.5 g/kg VO	Cancer cell lines	Antimutagenic Chemopreventive		+	F344 Rat colon ¹	+		Inhibitory effects on bacterial mutagenesis (salmonella assay) and aberrant crypt focus formation	Japan, Tokushima; 32. Chiampa-Nichayakul, 2001
Brown rice Phenols extracts of bran	Protocatechuic, p-coumaric, caffeic, feluirc, sinapic, vanillic, Tricin ; methoxycinnamic: < levels white Rice	Cancer cell lines	Chemopreventive			Breast, colon ⁶		+	Interference proliferation or colony forming ability. Decreased # of viable MDA MB 468 y HBL 100 breast cells; and colon derived SW 480 and human colonic epithelial cells	UK, Leicester; 33. Hudson EA, 2000
Rye bran Crude extract	Hydroxymatairesinol		Chemopreventive			Apc (Min) Mice:			Reduced number of adenomatous polyposis colimultiple neoplasia: effect mediated through Apc-beta-catenin pathway	Finland, Helsinki; 34. Oikarinen SI, 2000
260 extracts from 75 plants: Africa, Panama, Mauritius	Future identification. (used empirically by traditional healers)	Cancer cell lines	Cytotoxicity 3 different concentrations of each extract			Colon Co115		+	15 plant showed ED ₅₀ 10-1 mcg/ml. > significant 11 plant 1-0.1 mcg/ml. >3 plant 0.1-0.01 mcg/ml.	Switzerland, Lausanne; 35. Chapuis JC, 1988
Red pepper Na Cl Maejoo Ginseng Retinyl palmitate	As common foods		Co-carcinogenicity of Korean foods with methyl-nitro-nitrosoguanidine ⁹		+	ACI, Fisher, Sprague Dawley, Wistar Rats ⁸	+		Gastric carcinogenesis was enhanced by red pepper and high salt diet; was inhibited by maejoo and ginseng diet and was not affected by vitamin A	Korean, 36. Kim JP, 1985
Soybean extract	Containing bowman-birk protease inhibitor		Protective vs cancer		+	Rodents mice	+		Significant suppression of adenomatous tumors of the colonic mucosa	37. Wedd HG 1985
Standard diets supplemented with Peas, spinach, sprouts, brocoli			Quimioprotective effect is due to inhibition of promotion less than initiation	+	+	Rats ⁷	+		Reduced colorectal cancer and aberrant crypt. Not affect in situ. Carotenoids do not have effect (only marginal)	Netherlands, Vlaardingen; 38. Rijken PJ, 1999
Roselle <i>Hibiscus sabdariffa</i> Linn.	80% ethanolic extract (Thailand)		Antimutagenic Salmonella typhimurium			F344 Rats ^{1,10}			Reduces 60-90% mutagenicity Decreases aberrant crypt foci in colon, in the initiation stage; but increase # of ACF in the post-initiation stage.	Japan, Tokushima; 39. Chewonarin T, 1999
Garlic <i>Allium sativum</i> Powder, Extract or combination	8-10% L(+) – alliin Powder and extract were efficient vs lymphatic leukemia	Tumor cell lines proliferation, hepatoma and colon	Only combination, concentration-dependent inhibition cell growth IC50 330 mcg/ml for HepG2 and 480 vs Caco-2		+			+	Antiproliferative effects due to breakdown products of alliin (allicin and polysulfides) by the potentiation of powder (alliinase system) to an alliin enriched without alliinase (garlic extract) potentiated the effects observed	Germany, Luebeck; 40. Siegers CP, 1999

Table I. Continued

Common and scientific name; preparation	Active principle	Human	Chemoprotective effect	T	P	Animal and CA method	V	v	Actions	Country, City, First author, year
<i>Coptidis rhizoma</i> <i>Scutellariae radix</i> Aqueous extracts 2% of diet	Berberini and baicalein (as a control)		Antiinflammatory Chemopreventive		+	Male F344 Rat ¹	+		Inhibited AOM-induced ACF formation, 54 y 78 % <i>Coptidis</i> and <i>Scutellariae</i> , because inhibit COX-2 and COX-1, respectively	Japan, Ibaraki; 41. Fukutake M, 1998
Avemar (Weath germ extract) Avemar+vit C	Standarized benzoquinone	CA cell lines: Lewis lung Ca 3LL-HH; B16 melanoma, colon xenograft HCH25, and rat nephroblastoma	Immunostimulatory effect and it explain metastasis inhibiting effect		+	Mice immunosupressed artificially		+	Combined inhibited metastasis formation in all cell lines lines. Vitamin C alone not; Avemar along >inhibitory metastasis in certain lines	Hungary, Budapest; 42. Hidvegi M 1998
<i>Annona reticulata ethylacetate</i> extract seeds	Acetogenins	Cancer cell lines	Citotoxicity					+	Citotoxicity against Hep2.2.15, Hep G2, KB and CCM2	Taiwán, Koahsiung; 43. Chang FR, 1998
Lemon grass <i>Cymbopogon citratus</i> <i>Stapf</i> 80% ethanol extract			Antimutagenic Salmonella assay		+	F344 Rat colon ¹	+		inhibited DNA adduct formation by colonic mucosa and muscular layer, not in the liver; inhibited ACF in initiation stage and promotion stage; and fecal B-glucuronidase; and had antioxidant activity	Japan, Kuramoto-cho; 44. Suaeyun R, 1997
<i>Rhaphidophora korthalsii</i> Hot water extract		Cancer cell lines	Anticancerigen by cytotoxicity and immunomodulator		+			+	Cototoxicity Vs P388, Molt 4, KB, SW 620 Splencocytes stimulating activity:	Singapore. 45. Wong KT, 1996

1. Azoxymethane induced colonic aberrant crypt foci (AOM-ACF). 2. Phorbol 12-myristate 13-acetate- induced inflammatory responses (PMA). 3. Ornithine decarboxylase activity assay (ODC), epidermal. 4. Mouse ear swelling model: 12-O-Tetradecanoylphorbol-13-acetate (TPA); dinitrofluorobenzene (DNFB). 5. 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical assay. 6. Luminescent ATP cell viability assay. 7. MTT tetrazolium salt assay. T=treatment; P= preventive; V= *in vivo*; v = *in vitro*. 8. 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium assay. 9. Colorimetric assay to determine cell survival of human colon carcinoma Co 115. 10. MNNG 100 mcg/ml; 83 mcg/ml. 11. Dimethylhydrazine-induced adenomatous tumors mouse colon (DMH). 12. 2-amino-1-methyl-6-phenylimidazol [4,5-b] pyridine (PhIP) mutagenic. 13. Tripan blue dye exclusion assay. 14. Enzyme immunoassay (EIA). 15. Assay annexin V-propidium iodide. 16. Texas red-conjugated wheat germ agglutinin

RESULTS

Fifty-eight articles mentioned natural products with anticancer activity; of these, 13 were discarded because the principal focus of the work was not appropriate. In 45 articles, we cataloged common and scientific name, part of plant and/or its products used as treatment or preventive, used experimental *in vivo* or *in vitro* models, pharmacological effects and actions, human or animal species studied and apparent efficacy (Table I). Clinical studies were also of note.

We found more than 50 plants employed in these studies. The part of plants used varied among roots, bark, twig, rhizome, leaves, whole extracts as well as purified substances.

Our analyses showed that most studies (55%) used human cancer cell lines incubated with plant extracts as a model to look for cellular modifications from structural changes to cellular cycle interruption. In some studies (40%) animals were given tumors followed by treatment with several doses of the experimental plant extract. Efficacy was determined by reduction of the size and number of tumors by unit of area. Few articles were clinical studies (5%).

The pharmacological activities, which appear to explain the chemopreventive or anticancer effect are varied: antiproliferative, antitumor activity, anti-inflammatory and antiallergy; antioxidant, agent; antibacterial and cytotoxic; immunomodulatory; apoptosis plus photodynamic induction; anticancer *in vivo* or *in vitro*; apoptosis by cell cycle interruption; nucleosomal DNA fragmentation; scavenging activity; atipyretic, analgesic; antimutagenic in *Salmonella typhimurium*; and immunostimulatory activity explain metastasis inhibiting effects, and anticarcinogenic properties (Table I). Some products have more than one activity, and all these effects are responsible of inhibition of growth of the tumors [38]. Efficacy was determined by reduction of the size and number of tumors by unit of area [5,6].

Additionally we looked for which of these natural products were mentioned at the international literature and are included in a) the commercial information at Mexican marketing PLM; we found *Ginkgo biloba* as useful against brain circulatory insufficiency, but not mentioned its anticancer activity; and St. John wort *Hypericum perforatum* (different species from that in the literature); b) in the academic

Mexican book “Vademecum Académico de Medicamentos”, 2004: none are mentioned; c) in Goodman Gilman’s Pharmacology, 2001: only ginkgolide, derived from *Ginkgo biloba*, was mentioned as inhibitor of platelet-activating factor; and d) in Katzung book Medical Pharmacology there are three natural products, Garlic (*Allium sativum*) as antioxidant, antimicrobial and antineoplastic; Ginko (*Ginkgo biloba*) as antioxidant, antiplatelet and anti-inflammatory, but not as antineoplastics, and St. John Wort (*Hypericum perforatum*) as antidepressive, antiviral and antitumoral.

DISCUSSION

In this literature review, all the natural products experimentally studied showed some kind of pharmacological activity which could explain their capacity to act against cancer development. Although these studies tend to support the use of these plant products on an experimental basis carried out *in vitro* and *in vivo*, in animals, in humans and in human cancer cell lines, their use will require clinical evaluation. The absence of a discussion of the majority of these agents in pharmacology text books reflects the attitude of modern medicine. Renewed interest in traditional pharmacognosy suggest that a re-evaluation of the inclusion of natural products in pharmacology courses taught to medical and pharmacy students is in order. The availability of these plant products, particularly in Mexico warrants their academic re-evaluation.

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