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Review

Mexican medicinal plants used for cancer treatment: Pharmacological, phytochemical and ethnobotanical studies

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ABSTRACT

Aim of the study: This review provides a summary of Mexican medicinal flora in terms of ethnobotanical, pharmacology, and chemistry of natural products related to anticancer activity.
Materials and methods: Bibliographic investigation was carried out by analyzing recognized books and peer-reviewed papers, consulting worldwide accepted scientific databases from the last five decades. Mexican plants with attributed anti-cancer properties were classified into six groups: (a) plant extracts that have been evaluated for cytotoxic effects, (b) plant extracts that have documented anti-tumoral effects, (c) plants with active compounds tested on cancer cell lines, (d) plants with novel active compounds found only in Mexican species, (e) plants with active compounds that have been assayed on animal models and (f) plants with anti-cancer ethnopharmacological references but without scientific studies.
Results: Three hundred plant species belonging to 90 botanical families used for cancer treatment have been recorded, of which only 181 have been experimentally analyzed. The remaining 119 plant species are in use in empirical treatment of diseases consistent with cancer symptomatology. Only 88 of the plant extracts experimentally studied in *in vitro* cellular models have demonstrated active cytotoxic effects in at least one cancer cell line, and 14 out of the 88 have also been tested *in vivo* with the results that one of them demonstrated anti-neoplasic effects. A total of 187 compounds, belonging to 19 types of plant secondary metabolites, have been isolated from 51 plant extracts with active cytotoxic effects, but only 77 of these compounds (41%) have demonstrated cytoxicity. Seventeen of these active principles have not been reported in other plant species. However, only 5 compounds have been evaluated *in vivo*, and 3 of them could be considered as active.
Conclusion: Clearly, this review indicates that it is time to increase the number of experimental studies and to begin to conduct clinical trials with those Mexican plants and its active compounds selected by *in vitro* and *in vivo* activities. Also, the mechanisms of action by which plant extracts and their active compounds exert anti-cancer effects remain to be studied.

Contents

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1. Introduction

Chemotherapy and radiotherapy, the conventional cancer treatments used nowadays, are expensive and cause many side effects, including such minor ones as vomiting, alopecia, diarrhea, constipation, and major ones such as myelosuppression, neurological, cardiac, pulmonary and renal toxicity. All such side effects reduce the quality of life and discourage patients to observe medication protocols which then lead to the progression of cancer and associated complications. In addition, many of these treatments present limited anti-cancer activity (Mans et al., 2000). Resection surgery procedures, on the other hand, cause functional deficiencies or esthetic discomfort. Therefore, there is a need to discover alternative anticancer drugs, hopefully more potent, as well as more selective and less toxic than those currently in use.

Approximately 60% of drugs currently used for cancer treatment have been isolated from natural products (Gordaliza, 2007) and the plant kingdom has been the most significant source. These include *Vinca* alkaloids, *Taxus* diterpenes, *Camptotheca* alkaloids, and *Podophyllum* lignans. Currently, there are 16 new plant-derived compounds being tested in clinical trials and of these 13 are being tested in phase I or II, and 3 are in phase III. Among these compounds, flavopiridol, isolated from the Indian tree *Dysoxylum binectariferum*, and mesoindigo, isolated from the Chinese plant *Indigofera tinctoria*, have been shown to exhibit anti-cancer effects with lesser toxicity than conventional drugs (Saklani and Kutty, 2008).

The initial screenings for plants used for cancer treatment are cell-based assays using established cell lines, in which the toxic effects of plant extracts or isolated compounds can be measured. According to the National Cancer Institute (NCI), plant extracts and pure compounds with cytotoxic ED_{50} (Effective Dose 50) values $\leq$30 μg/ml and $\leq$4 μg/ml, respectively, are considered active (Suffness and Pezzuto, 1990). Cytotoxic screening models supply important preliminary data to select plant extracts or compounds with potential antineoplastic properties. In addition, cytotoxic assays do not provide false negative results since they consider plant extracts or compounds which affect cell viability. Most of the clinically used antitumor agents possess significant cytotoxic activity in cell culture systems. In most cases, the cytotoxic effects of Mexican plant extracts and their isolated compounds have been studied employing established cancer cell lines, and few reports have used primary cultures derived from human or animal tumors (Johansson et al., 2003), or drug-resistant-induced cell lines (Villarreal et al., 1992; Novelo et al., 1993; Pereda-Miranda et al., 1993; Villarreal et al., 1994; Wickramaratne et al., 1995). The use of these cell lines mentioned above might provide a more accurate screening of the toxic effects of plant extracts and their active compounds. Because cancer drug-resistance is a significant health problem, it is necessary to carry out more studies addressing this topic. In addition, studies of the toxicological effects of plant extracts and their isolated compounds on normal cells should be included. Canine kidney (MDCK), mouse fibroblasts (L929), Rhesus monkey kidney from *Macaca mullata* cells (LLC-MK2) and human peripheral blood mononuclear cells (Sanchez et al., 2001; Franco-Molina et al., 2003; Mena-Rejon et al., 2009) have been used as normal cells in cytotoxic studies.

Extracts or compounds that are found to be active in the *in vitro* models are then tested for their efficacy through *in vivo* studies. *In vivo* models, in which tumors are induced, using NOD-SCID, Balb C57BL/6, and athymic mice, are widely employed for these studies.

The main strategies for the selection of plant species in cancer drug discovery include random screening, chemotaxonomic information and ethnomedical knowledge. Random screening is employed when the number of candidates is low and/or the research means are ample (Lautié et al., 2008). Chemotaxonomy distinguishes related species by their production of different secondary metabolites, different ecological features and different physiological characteristics. Ethnobotanical knowledge includes plants used in the traditional medical systems such as herbalism, folklore and shamanism. The preparation procedures indicated in these systems can suggest the best extraction method.

In this review, local and international literatures were used to search for the *in vitro* and *in vivo* effects of Mexican plants and their active compounds used to treat conditions consistent with cancer symptomatology, and medicinal plants used empirically in the treatment of diseases with cancer symptomatology without scientific studies. We also present information about novel compounds, isolated from Mexican plant extracts with cytotoxic and anti-neoplastic properties.

The terminology used in this review is based on the definitions suggested by Suffness and Douros (1982). "Cytotoxicity" indicates that an extract or compound shows activity against cancer cell lines. "anti-tumor" or "anti-neoplastic" indicates that a plant or compound is effective *in vivo*. Finally, "anti-cancer" refers to compounds that are clinically active against human cancer.

Since the term "cancer" is not well defined in traditional Mexican medicine, and has been applied to describe general conditions such as inflammations, ulcers or dermatological conditions such as "hard swellings", abscesses, calluses, corns, warts, polyps; it is not an easy task to discover anticancer drugs using the ethnobotanical approach. However it is important to review the existing literature that could indicate connections between ethnobotanical data to experimental *in vivo* or *in vitro* models, indicating an approach to select plant candidates for scientific investigation.

2. Use of medicinal plants as a complementary and alternative medicine for cancer

Medicinal plants constitute a common alternative for cancer treatment in many countries around the world (Gerson-Cwilich et al., 2006; Tascilar et al., 2006). At this time, more than 3000 plants worldwide have been reported to have anti-cancer properties (Graham et al., 2000). Globally, the incidence of use of plant-derived products for cancer treatment is from 10% to 40% with this rate reaching 50% in Asiatic patients (Cassileth and Deng, 2004; Tascilar et al., 2006; Molassiotis et al., 2006). In Europe, the expenditures for anti-cancer herbal products are estimated to be 5 billion dollars per year (Tascilar et al., 2006).

Table 1A
Ethnomedical uses of Mexican plants employed empirically for cancer treatment with scientific reports.

Family	Scientific name	Popular use	Reference
Acanthaceae	*Justicia spicigera* Schltdl.	GI, WOM, CC	Vega-Avila et al. (2009)
Agavaceae	Agave *salmiana* Otto ex Salm-Dyck	INF DER, ST	Popoca et al. (1998)
Anacardiaceae	*Amphipterygium adstringens* (Schltdl.) Standl.	VEN, CC	Villarreal et al. (1992)
Annonaceae	*Annona diversifolia* Saff.	GI, INF, ST	Schlie-Guzmán et al. (2009)
	Annona muricata L.	GI, GC	Martínez (1989)
	Annona purpurea Moc. & Sessé ex Dunal	INF, ST	Chávez and Mata (1998)
	Rollinia mucosa (Jacq.) Baill.	INF, ST	Chávez et al. (1998)
Apocynaceae	*Thevetia ahouai* (L.) A. DC.	INF, GI, ST	Cabrera (1958)
Araliaceae	*Dendropanax arboreus* (L.) Decne. & Planch.	INF, BC	Hernández (1959)
Aristolochiaceae	*Aristolochia brevipes* Benth.	INF, DER, ST	Martínez (1989)
Asteraceae	*Bidens pilosa* L.	WOM, UR, CC	Villavicencio-Nieto et al. (2008)
	Gnaphalium purpureum L.	GI, RES, ST	López and Hinojosa (1988)
	Gymnosperma glutinosum (Spreng.) Less.	INF, ST	Gomez-Flores et al. (2009)
	Haplopappus spinulosus subsp. *scabrellus* (Greene) H. M. Hall	GI, DER, ST	Hernández (1959)
	Helianthella quinquenervis (Hook) A. Gray	GI, GC	Castañeda et al. (1996)
	Heterotheca inuloides Cass.	DER, ST	Villarreal et al. (1992)
	Hymenoxys odorata DC.	GI, DER, ST	Ivie et al. (1975)
	Iostephane heterophylla (Cav.) Hemsl.	GI, DER, ST	Aguilar et al. (2001)
	Montanoa leucantha (Lag.) S. F. Blake	VEN, CC	Oshima et al. (1986)
	Psacalium peltatum (Kunth) Cass.	INF, DER, UR, ST	Velasco et al. (2005)
	Roldana angulifolia (D.C.) H. Rob. & Brettell	INF, ST	Arciniegas et al. (2006)
	Roldana sessilifolia (Hook. & Am.) H. Rob. & Brettel	WOM, DER, ST	Villarreal et al. (1994)
	Schkuhria schkuhrioides Thell.	DER, ST	Delgado et al. (1998)
	Smallanthus maculatus (Cav.) H. Rob.	GI, GC	Rios and León (2006)
	Tagetes lucida Cav.	GI, GC	Hernández (1959)
	Tithonia diversifolia (Hemsl.) A. Gray	GI, DER, ST	Del Amo (1979)
	Verbesina persicifolia DC.	INF, GI, GC	Hernández (1959)
	Viguiera decurrens (A. Gray)	INF, GI, GC	Marquina et al. (2001)
	Viguiera hypargyrea Greenm.	GI, DER, GC	Villarreal et al. (1994)
	Viguiera lactibracteata (Hemsl.) Blake	GI, GC	Villarreal et al. (1994)
	Viguiera quinqueradiata (Cav.) A. Gray	GI, GC	Villarreal et al. (1994)
Betulaceae	*Alnus jorullensis* Kunth subsp. *Jorullensis*	GI, GC	López and Hinojosa (1988)
Bignoniaceae	*Astianthus viminalis* (Kunth) Baill.	UR, INF DER, ST	Villarreal et al. (1992)
	Crescentia alata Kunth	GI, DER, ST	Hernández (1959)
	Jacaranda mimosifolia D. Don	AP, ST	Villarreal et al. (1992)
Bixaceae	*Bixa orellana* L.	DER, ST	Hernández (1959)
	Cochlospermum vitifolium (Willd.) Spreng.	GI, DER, ST	López and Hinojosa (1988)
Boraginaceae	*Heliotropium curassavicum* var. *oculatum* (A. Heller) I. M. Johnst. ex Tidestr.	DER, GI, GC	Hernández (1959)
Burseraceae	*Bursera bipinnata* (DC.) Engl.	DER, ST	Lautié et al. (2008)
	Bursera copallifera (DC.) Bullock	DER, ST	Lautié et al. (2008)
	Bursera fagaroides var. *elongata* McVaugh & Rzed.	VEN, DER, ST	Murillo-Alvarez et al. (2001)
	Bursera grandifolia (Schltdl.) Engl.	DER, ST	Wickramaratne et al. (1995)
	Bursera graveolens (Kunth) Triana & Planch.	INF, ST	Nakanishi et al. (2005)
Cactaceae	*Pachycereus webery* (J. M. Coult.) Backeb.	GI. DER, ST	Popoca et al. (1998)
Capparidaceae	*Polanisia dodecandra* (L.) DC.	DER, ST	Shi et al. (1995)
Caprifoliaceae	*Viburnum jucundum* C. V. Morton	GI, GC	Rios et al. (2001)
Celastraceae	*Hippocratea excelsa* Kunth	INF, GI, GC	Popoca et al. (1998)
Commelinaceae	*Tradescantia discolor* L' Hér	RES, INF, DER, ST	Mena-Rejon et al. (2009)
	Tradescantia zebrina Bosse var. *Zebrina*	GI, GC	Frei et al. (1998)
Convolvulaceae	*Ipomoea murucoides* Roem. et Schult.	DER, ST	Chérigo and Pereda-Miranda (2006)
	Ipomoea orizabensis (Pelletan) Ledeb. ex Steud.	GI, DER, ST	Hernández-Carlos et al. (1999)
	Ipomoea pauciflora M. Martens & Galeotti	DER, ST, NEU	Villarreal et al. (1992)
Cucurbiataceae	*Ibervillea sonorae* (S. Watson) Greene	DER, UR, ST	Vega-Avila et al. (2009)
Cupressaceae	*Juniperusdeppeana* Steud.	INF, CC	Villavicencio-Nieto et al. (2008)
Euphorbiaceae	*Croton reflexifolius* Kunth	DER, ST	Ankli et al. (2002)
	Euphorbia pulcherrima Willd. ex Klotzsch	DER, ST	Villarreal et al. (1992)
	Jatropha gaumeri Greenm.	DER, ST	Ankli et al. (2002)
	Jatropha neopauciflora Pax	INF, DER, ST	García and Delgado (2006)
Fabaceae	*Acaciella angustissima* (Mill.) Britton & Rose	INF, DER, ST	Mena-Rejon et al. (2009)
	Acacia pennatula (Schltdl. & Cham.) Benth.	INF, ST	Popoca et al. (1998)
	Albizia occidentalis Brandegee	INF, ST	Cabrera (1958)
	Havardia albicans (Kunth) Britton & Rose	VEN, CC	Mena-Rejon et al. (2009)
	Mimosa tenuiflora (Willd.) Poir.	DER, ST	Villarreal et al. (1992)
	Pithecellobium unguis-cati (L.) Benth.	GI, DER, ST	Martínez (1989)
	Senna occidentalis (L.) H. S. Irwin & Barneby	INF, UR, DER, ST	Martínez (1989)
	Senna racemosa (Mill) H.S. Irwin & Barneby	GI, INF, DER, ST	Mena-Rejon et al. (2009)
Gelsemiaceae	*Gelsemium sempervirens* (L.) J. St.-Hil.	INF, ST	Schun and Cordell (1987)
Geraniaceae	*Geranium niveum* S. Watson	UR, DER, ST	Martínez (1989)
Krameriaceae	*Krameria pauciflora* DC.	GI, GC	Frei et al. (1998)
Lamiaceae	*Hyptis emory* Torr.	RES, GI, GC	López and Hinojosa (1988)
	Hyptis pectinata (L.) Poit.	GI, INF, DER, ST	Pereda-Miranda et al. (1993)
	Hyptis spicigera Lam.	INF, DER, ST	Fragoso-Serrano et al. (1999)
	Hyptis suaveolens (L.) Poit.	GI, DER, ST	Lautié et al. (2008)
	Hyptis verticillata Jacq.	GI, DER, ST	Novelo et al. (1993)
	Salvia pachyphylla Epling ex Munz	GI, RES, GC	Martínez (1989)

Table 1A (*Continued*)

Family	Scientific name	Popular use	Reference
Lauraceae	*Persea americana* Mill.	INF, DER, ST	Andrade-Cetto (2009)
Linaceae	*Linum scabrellum* Planch.	GI, DER, ST	Lautié et al. (2008)
Lythraceae	*Cuphea aequipetala* Cav.	DER, ST	Vega-Avila et al. (2004)
Loranthaceae	*Cladocolea grahamii* (Benth.) Tieg.	UR, DER, ST	Waizel-Bucay et al. (1994)
Malvaceae	*Gossypium hirsutum* L.	DER, INF, ST	Mena-Rejon et al. (2009)
Meliaceae	*Swietenia humilis* Zucc.	GI, INF, DER, ST	Graham et al. (2000), Camacho et al. (2003)
Moraceae	*Dorstenia contrajerva* L.	GI, DER, ST	Martínez (1989)
Myrtaceae	*Psidium guajava* L.	GI, ST	Villarreal et al. (1992)
Orchidaceae	*Vanilla planifolia* Andrews	UR, DER, ST	Hernández (1959)
Papavaraceae	*Bocconia frutescens* L.	RES, GI, GC	Hernández (1959)
Phizophoraceae	*Rhizophora mangle* L.	INF, DER, ST	Mena-Rejon et al. (2009)
Phytolaccaceae	*Petiveria alliacea* L.	INF, DER, ST	Perez-Leal et al. (2006)
Picramniaceae	*Alvaradoa amorphoides* Liebm.	DER, ST	Martínez (1989)
	Castela tortuosa Liebm.	AP, GC	Villarreal et al. (1992)
	Picramnia antidesma subsp. *fessonia* (DC.) W. W. Thomas	VEN, DER, ST	Martínez (1989)
Piperaceae	*Piper aduncum* L.	UR, DER, ST	Martínez (1989)
Plumbaginaceae	*Plumbago pulchella* Boiss.	DER, ST	Martínez (1989)
Poaceae	*Zea mays* L.	UR, GI, GC	Hayashi et al. (1996)
Rhamnaceae	*Colubrina macrocarpa* (Cav.) G. Don	GI, RES, GC	Popoca et al. (1998)
Rubiacaeae	*Hamelia patens* Jacq.	INF, DER, WOM, CC	Mena-Rejon et al. (2009)
	Hintonia latiflora Sessé & Moc. ex DC. Bullock	INF, GI, GC	López and Hinojosa (1988)
	Morinda royoc L.	DER, ST	Martínez (1989)
Sapotaceae	*Chrysophyllum mexicanum* Brandegee ex Standl.	GI, GC	Ankli et al. (2002)
	Manilkara zapota (L.) Van Royen	GI, GC	Ma et al. (2003)
Scrophulariaceae	*Capraria biflora* L.	UR, CC	Del Amo (1979)
Smilacaceae	*Smilax aristolochiifolia* Mill.	INF, GI, GC	Linares-Mazari et al. (1988)
Solanaceae	*Capsicum annum* L.	AP, GI, GC	Argueta et al. (1994)
	Cestrum nocturnum L.	GI, INF, DER, ST	Del Amo (1979)
	Solanum chrysotrichum Schltdl.	DER, ST	Villarreal et al. (1992)
	Solanum lanceolatum Cav.	GI, DER, ST	Frei et al. (1998)
	Solanum rostratum Dun.	GI, WOM, CC	Villavicencio-Nieto et al. (2008)
Verbenaceae	*Lantana involucrata* L.	INF, ST	Del Amo (1979)
	Lantana urticifolia Mill.	GI, GC	López and Hinojosa (1988)
Viscaceae	*Phoradendron carneum* Urb.	UR, DER, ST	Martínez (1989)
	Phoradendron galeottii Trel.	UR, DER, ST	Waizel-Bucay et al. (1994)
	Phoradendron reichenbachianum (Seem.) Oliver	UR, DER, ST	Rios et al. (2001)
	Phoradendron serotinum (Raf.) M. C. Johnst.	UR, DER, ST	Johansson et al. (2003)
Zamiaceae	*Dioon spinulosum* Dyer ex Eichl	GI, GC	Mena-Rejon et al. (2009)
Zygophyllaceae	*Larrea tridentata* (DC.) Cav.	UR, GI, GC	Gonzalez (1984)

Popular use: AP, antiparasitic; BC, breast cancer; CC, cervical cancer; DER, dermatological conditions; GC, gastric cancer; GI, gastrointestinal disorders; INF, inflammatory diseases; NEU, neurological disorders; RES, respiratory illnesses; ST, skin tumors; UR, urological problems including diabetes; VEN, venereal diseases; WOM, gynecological disorders.

In Mexico, more than 90% of the general population use medicinal plants in common practice for the empirical treatment of several diseases (Taddei-Bringas et al., 1999). However, most physicians disagree with the use of plant products because they lack toxicological and pharmacological studies. In urban areas, prescriptions for medicinal plants are done by vendors of herbal products, whereas in rural areas the populations refer to the local healers, "chamanes", to receive treatment. In Mexico, 30–70% of patients diagnosed with cancer use herbal extracts as an alternative therapy for many types of cancer in urban areas (Gerson-Cwilich et al., 2006; Gomez-Martinez et al., 2007). Nevertheless, limited data is available concerning cost and/or the effectiveness of herbal extracts. Cancer patients perceive the medicinal plants to be efficient and safe because of their "natural" origin, even when they do know of the lack of scientific evidence (Gerson-Cwilich et al., 2006). As a consequence, patients often use herbal remedies without biomedical medication, or in some cases combined with anti-cancer drugs without advising their physicians (Gomez-Martinez et al., 2007). This constitutes a health risk because these products, which contain several constituents, could interact with the prescribed drugs and affect drug metabolic pathways.

3. Sources of information on Mexican plants used for cancer treatment

A bibliographic investigation was carried out, during September 2009 to March 2010, by analyzing commonly consulted scientific books in México, local encyclopedias of the Mexican Institute for Indigenous Studies (INI), and scientific published material on native Mexican medicinal flora from the last five decades for the ethnobotanical, pharmacological, and chemical characterization of natural products. Peer-reviewed articles were gathered consulting the databases SCOPUS, Web of Science, SCIELO, Medline and Google scholar. The following keywords were used to search for the literature inside the databases: plant extract, anticancer, México, and cytotoxic compounds. No restrictions regarding the language of publication were imposed, but most relevant studies were published in English and Spanish. The criteria followed for selection of reports in this review consider those plants (i) native to Mexico, and in some cases also to other countries in the Americas, (ii) used in Mexican traditional medicine, (iii) with experimental studies on anticancer effects, (iv) with ED_{50} values reported in mass/volume, (v) with information obtained from a clear source, (vi) with animal studies for antitumor effects and (vii) with studies exploring mechanisms of anticancer effects. Mexican plants with attributed anti-cancer properties are classified into six groups: (a) plant extracts that have been evaluated for cytotoxic effects, (b) plant extracts that have documented anti-tumoral effects, (c) plants with active compounds tested on cancer cell lines, (d) plants with novel active compounds found only in Mexican species, (e) plants with active compounds that have been assayed on animal models and (f) plants with anticancer ethnopharmacological references but without scientific studies.

Table 1B
Ethnomedical uses of Mexican plants not employed empirically for cancer treatment but with scientific reports.

Family	Scientific name	Popular use	Reference
Acanthaceae	*Elytraria imbricata* (Vahl.) Pers.	GI	Encarnacion and Contreras (1992)
Agavaceae	*Agave americana* L.	UR	Yokosuka et al. (2000)
Annonaceae	*Mosannona depressa* (Baill.) Chatrou	INF	Jimenez-Arellanes et al. (1996)
Apocynaceae	*Pentalinon andrieuxii* (Mûll. Arg.) B. F. Hansen & Wunderlin	AP	Chan-Bacab et al. (2003)
Araceae	*Xanthosoma robustum* Schott	DER	Frei et al. (1998)
Aristolochiaceae	*Aristolochia monticola* Brandegee	GI	Encarnacion and Contreras (1992)
Asclepiadaceae	*Asclepias subulata* Decne.	GI	Encarnacion and Contreras (1992)
Asteraceae	*Adenophyllum aurantium* (L.) Strother	GI	Frei et al. (1998)
	Ambrosia monogyra (Torr. & A. Gray) Strother & B. G. Baldwin	AP	Murillo-Alvarez et al. (2001)
	Baccharis salicifolia (Ruiz & Pav.) Pers.	WOM, INF, RES	Hernández (1959)
	Bidens squarrosa Kunth	GI	Ankli et al. (2002)
	Epaltes mexicana Less.	RES	Frei et al. (1998)
	Melampodium paniculatum Gardner	GI	Martínez (1989)
	Neurolaena lobata (L.) Cass	GI	Martínez (1989)
	Parthenium argentatum Gray	GI	Parra-Delgado et al. (2005)
	Pectis haenkeana (DC.) Sch. Bip.	GI	Hernández (1959)
	Pseudognaphalium semiamplexicaule (DC.) Anderb.	RES, DER	Sanchez et al. (2001)
	Ratibida latipalearis E.L. Richards	DER	Camacho et al. (2003)
	Ratibida mexicana (S. Watson) W.M. Sharp	GI	Camacho et al. (2003)
	Xylotamia diffusa (Benth.) G. L. Nesom	DER, RES	Murillo-Alvarez et al. (2001)
Begoniaceae	*Begonia heracleifolia* Schltdl. & Cham.	INF	Martínez (1989)
Bignoniaceae	*Tecoma stans* (L.) Juss. ex Kunth	UR	Marzouk et al. (2006)
Boraginaceae	*Cordia curassavica* (Jacq.) Roem. ex Schult.	INF	Hernández (1959)
Brassicaceae	*Descurainia pinnata* subsp. *menziesii* (DC.) Detling	GI	Encarnacion and Contreras (1992)
Bromeliaceae	*Aechmea bracteata* var. *bracteata* Griseb.	DER	Ankli et al. (2002)
	Bromelia pinguin L.	UR	Raffauf et al. (1981)
Cactaceae	*Lophophora williamsii* (Lem. ex Salm-Dyck) J.M. Coult	GI, UR	Franco-Molina et al. (2003)
Campanulaceae	*Lobelia laxiflora* Kunth	INF, RES	Hernández (1959)
Caprifoliaceae	*Valeriana sorbifolia* Kunth	NEU	Xu et al. (2007)
Caricaceae	*Carica papaya* L.	GI	López and Hinojosa (1988)
Celastraceae	*Crossopetalum gaumeri* (Loes.) Lundell	GI	Ankli et al. (2002)
Combretaceae	*Combretum fruticosum* (Loefl.) Stuntz	DER	Martínez (1989)
Convolvulaceae	*Ipomoea pes-caprae* (L.) R. Br.	UR	Pereda-Miranda et al. (2005)
	Ipomoea stans Cav.	UR, NEU	Martínez (1989)
	Ipomoea wolcottiana subsp. *Wolcottiana*	DER	León et al. (2006)
Ebenaceae	*Diospyros anisandra* S. F. Blake	DER	Ankli et al. (2002)
	Diospyros digyna Jacq.	DER	Cabrera (1958)
	Diospyros tetrasperma Sw.	DER	Ankli et al. (2002)
Ericaceae	*Comarostaphylis polifolia* (Kunth) Zucc. ex Klotzsch	UR, RES	Hernández (1959)
Fabaceae	*Bauhinia divaricata* L.	GI, RES	Martínez (1989)
	Caesalpinia gaumeri Greenm.	DER	Hernández (1959)
	Calliandra californica Benth.	UR	Encarnación-Dimayuga et al. (2006)
	Dalea carthagenensis var. *barbata* (Oerst.) Barneby	DER	Ankli et al. (2002)
	Dialium guianense (Aubl.) Sandwith	INF	Cabrera (1958)
	Eysenhardtia polystachya (Ortega) Sarg.	UR	Alvarez et al. (1998)
	Leucaena leucocephala (Lam.) de Wit subsp. *leucocephala*	GI	Hernández (1959)
	Phaseolus acutifolius A. Gray	DER	Martínez (1989)
	Phaseolus vulgaris L.	DER, GI	Aparicio-Fernández et al. (2006)
	Piscidia piscipula (L.) Sarg.	INF, NEU	Martínez (1989)
	Vachellia campechiana (Mill.) Seigler & Ebinger	INF	Martínez (1989)
Hypericaceae	*Hypericum silenoides* Juss. subsp. *silenoides*	INF	Del Amo (1979)
Lamiaceae	*Salvia leucantha* Cav.	RES, GI	Aoyagi et al. (2008)
Loranthaceae	*Psittacanthus calyculatus* (DC.) G. Don	DER	Frei et al. (1998)
Malpighiaceae	*Galphimia glauca* Cav.	INF	Aguilar-Santamaría et al. (2007)
Malvaceae	*Luehea alternifolia* (Mill.) Mabb.	DER	Ankli et al. (2002)
Meliaceae	*Swietenia macrophylla* King	INF	Camacho et al. (2003)
Moraceae	*Dorstenia drakena* L.	DER	Frei et al. (1998)
Myrtaceae	*Psidium sartorianum* (O. Berg) Krug & Urb.	GI	Ankli et al. (2002)
Orchidaceae	*Stenorhynchus lanceolatus* (Aubl.) L. C. Rich.	INF	Camacho et al. (2003)
Picrodendraceae	*Piranhea mexicana* (Standl.) Radcl.-Sm.	DER	Camacho et al. (2003)
Pinaceae	*Pinus patula* Schltdl. & Cham.	DER, RES	Martínez (1989)
Polypodiaceae	*Microgramma nitida* (J. Sm.) A. R. Sm.	GI	Ankli et al. (2002)
Primulacaceae	*Bonellia macrocarpa* subsp. *pungens* (A. Gray) B. Stahl & Kâllersjô	INF	Del Amo (1979)
Rubiaceae	*Nernstia mexicana* (Zucc. & Mart. ex DC.) Urb.	GI	Camacho et al. (2003)
Rutaceae	*Casimiroa tetrameria* Millsp.	GI	Ankli et al. (2002)
Salicaceae	*Casearia nitida* (L.) Jacq.	INF	Ankli et al. (2002)
Verbenaceae	*Citharexylum ellipticum* D. Don	DER	Del Amo (1979)

Popular use: AP, antiparasitic; DER, dermatological conditions; GI, gastrointestinal disorders; INF, inflammatory diseases; NEU, neurological disorders; RES, respiratory illnesses; UR, urological problems including diabetes; VEN, venereal diseases; WOM, gynecological disorders.

4. Mexican plants with anti-cancer uses

Mexico has great botanical diversity and widespread use of traditional medicine based on herbolary; however, only a relatively small number of these plants have been subjected to accepted scientific evaluation for their potential anti-cancer effects. A total of 300 plants, belonging to 90 botanical families, with scientific and non-scientific evidence have been recorded, of which 181

Table 2
Cytotoxicity of Mexican plant extracts.

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
Acanthaceae	*Elytraria imbricata* (Vahl) Pers.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Justicia spicigera Schltdl.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001), Vega-Avila et al. (2009)
			EtOH	0.43 (T-47D), 5.59 (HeLa)	
		Lv	H_2O	14.79 (T-47D), NA (HeLa)	
Agavaceae	*Agave salmiana* Otto ex Salm-Dyck	Lv	PE	NA (HCT-15), NA (KB), NA (UISO)	Popoca et al. (1998)
			EtOAc	NA (HCT-15), NA (KB), NA (UISO)	
			MeOH	NA (HCT-15), NA (KB), NA (UISO)	
Anacardiaceae	*Amphipterygium adstringens* (Schltdl.) Standl.	Sb	EtOH	NA (KB), 8.5 (P-388), NA (KB-VI*)	Villarreal et al. (1992), Oviedo-Chávez et al. (2004)
			Chl	NA (KB), 17.4 (P-388), NA (KB-VI*)	
		Bk	PE	NA (KB), NA (P-388), NA (KB-VI*)	
			Hex	13.7 (HCT-15), 7.9 (MCF-7), NA (U-251), NA (PC-3), 8.4 (K-562)	
Annonaceae	*Annona muricata* L.	Lv	EtOH	6.2 (MCF-7), 4.0 (H-460), 8.5 (SF-268)	Calderon et al. (2006)
	Annona purpurea Moc. & Sessé ex Dunal	Sd	Chl:MeOH	0.01 (A-549), 1.53 (MCF-7), 1.47 (HT-29), 3.53 (A-498), 1.16 (PC-3), 0.02 (PACA-2)	Chávez and Mata (1998), Camacho et al. (2003)
		Bk	MeOH	0.0098 (KB)	
		Sm	H_2O	NA (A-549)	
			MeOH	1×10^{-4} (A-549)	
			H_2O	NA (A-549)	
	Mosannona depressa (Baill.) Chatrou	Sb	Chl	30 (A-549), 21 (MCF-7), 21 (HT-29)	Jimenez-Arellanes et al. (1996)
Apocynaceae	*Pentalinon andrieuxii* (Mûll. Arg.) B. F. Hansen & Wunderlin	Rt	MeOH	NA (KB), NA (UISO), NA (COLON)	Chan-Bacab et al. (2003)
		Lv		NA (OVCAR), NA (KB), 13.8 (UISO), NA (COLON)	
		Rt		5.4 (OVCAR), 2.6 (KB), 1.2 (UISO), 4.6 (COLON)	
	Thevetia ahouai (L.) A. DC.	St	EtOH	0.47 (MCF-7), 0.29 (H-460), 0.52 (SF-268)	Calderon et al. (2006)
Araceae	*Xanthosoma robustum* Schott	Lv	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
Araliaceae	*Dendropanax arboreus* (L.) Decne.& Planch.	Lv	EtOH	NA (MCF-7), NA (H-460), NA (SF-268)	Calderon et al. (2006)
Aristolochiaceae	*Aristolochia brevipes* Benth.	Ap	EtOH	19.7 (HCT-116)	Murillo-Alvarez et al. (2001)
	Aristolochia monticola Brandegee	Ap	EtOH	1.0 (HCT-116)	Murillo-Alvarez et al. (2001)
Asclepiadaceae	*Asclepias subulata* Decne.	Ap	EtOH	0.4 (HCT-116)	Murillo-Alvarez et al. (2001)
Asteraceae	*Adenophyllum aurantium* (L.) Strother	Lv	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
	Ambrosia monogyra (Torr. & A. Gray) Strother & B. G. Baldwin	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Baccharis salicifolia (Ruiz & Pav.) Pers.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Bidens pilosa L.	Bk	EtOH	NA (HeLa)	Murillo-Alvarez et al. (2001), Villavicencio-Nieto et al. (2008)
		Ap	EtOH	NA (HCT-116)	
	Bidens squarrosa Kunth	Ap	BuOH	NA (KB)	Ankli et al. (2002), Abbott et al. (1966)
		Wp	H_2O	NA (KB)	
	Epaltes mexicana Less.	Lv	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
	Gnaphalium purpureum L.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Gymnosperma glutinosum (Spreng.) Less.	Lv	Hex	4 (L5178Y-R)	Gomez-Flores et al. (2009)
	Haplopappus spinulosus subsp. *scabrellus* (Greene) H. M. Hall	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Helianthella quinquenervis (Hook) A. Gray	Rt	MeOH	3 (MCF-7), NA (HT-29), 5 (A-549)	Castañeda et al. (1996)
	Heterotheca inuloides Cass.	Fw	EtOH	NA (KB), 9.12 (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	15.13 (P-388), NA (KB-VI*)	
			PE	8.4 (P-388), NA (KB-VI*)	
	Iostephane heterophylla (Cav.) Hemsl.	Rt	Chl	NA (HCT-15), NA (UISO), NA (KB)	Aguilar et al. (2001)
			EtOH	NA (HCT-15), NA (UISO), NA (KB)	
	Melampodium paniculatum Gardner	Sm	EtOH	8.5 (MCF-7), 8.4 (H-460), NA (SF-268)	Calderon et al. (2006)
	Montanoa leucantha (Lag.) S. F. Blake	Lv	EtOAc	1.35 (KB), 5.2 (P-388)	Oshima et al. (1986)
	Neurolaena lobata (L.) Cass	Lv	EtOH	NA (MCF-7), NA (H-460), NA (SF-268)	Calderon et al. (2006)
	Pectis haenkeana (DC.) Sch. Bip.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Psacalium peltatum (Kunth) Cass.	Rt and Rh	H_2O	NA (DU-145)	Velasco et al. (2005)
			Hex	NA (DU-145)	
			Dcl	NA (DU-145)	
			MeOH	NA (DU-145)	
	Ratibida latipalearis E.L. Richards	Ap	MeOH	NA (KB)	Camacho et al. (2003)
	Ratibida mexicana (S Watson) WM Sharp	Ap	MeOH	NA (KB)	Camacho et al. (2003)
	Schkuhria schkuhrioides Thell.	Ap	Aco	NA (KB), NA (UISO), NA (COLON)	Delgado et al. (1998)
	Smallanthus maculatus (Cav.) H. Rob.	Ap	Aco	17 (HCT-15), 18.4 (OVCAR-5)	Rios and León (2006)
	Tagetes lucida Cav.	Ap	EtOH	1.82 (T-47D), NA (HeLa)	Vega-Avila et al. (2009)

Table 2 (*Continued*)

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
			H_2O	18.94 (T-47D), 13.2 (HeLa)	
	Tithonia diversifolia (Hemsl.) A. Gray	Lv	EtOH	NA (MCF-7), NA (H-460), NA (SF-268)	Calderon et al. (2006)
	Verbesina persicifolia DC.	Ap	H_2O	5.5 (KB)	Abbott et al. (1966)
	Viguiera decurrens (A. Gray)	Rt	Hex–EtOAc–MeOH	NA (KB), 2.3 (P-388), 8.9 (OVCAR), NA (COLON), 3.02 (UISO)	Marquina et al. (2001)
	Xylotamia diffusa (Benth.) G. L. Nesom	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
Begoniaceae	*Begonia heracleifolia* Schltdl. & Cham.	Rh	EtOH	3.8 (KB), 7.5 (Caco-2)	Frei et al. (1998)
Betulaceae	*Alnus jorullensis* Kunth subsp. *jorullensis*	Bk	H_2O	5.6 (KB)	Abbott et al. (1966)
Bignoniaceae	*Astianthus viminalis* (Kunth) Baill.	Lv	EtOH	NA (KB), NA (P-388), NA (KB-VI*)	Villarreal et al. (1992)
	Crescentia alata Kunth	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
	Jacaranda mimosifolia D. Don	Lv	EtOH	15.8 (KB), 1.6 (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	3.9 (P-388), 6.7 (KB-VI*)	
			PE	10.9 (KB), 1.2 (P-388), NA (KB-VI*)	
	Tecoma stans (L.) Juss. ex Kunth	Ap	EtOH:Chl	NA (KB)	Abbott et al. (1966), Marzouk et al. (2006)
		Fw and Ft	EtOH	NA (Hep-G2), NA (MCF-7), NA (1301)	
Bixaceae	*Bixa orellana* L.	wp	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
	Cochlospermum vitifolium (Willd.) Spreng.	Ft	H_2O	3.8 (KB)	Abbott et al. (1966)
			EtOH:Chl	3.2 (KB)	
		Fw	EtOH:Chl	5.0 (KB)	
Boraginaceae	*Cordia curassavica* (Jacq.) Roem. ex Schult.	Lv	EtOH	5.9 (MCF-7), 5.7 (H-460), 8.2 (SF-268)	Calderon et al. (2006)
	Heliotropium curassavicum var. *oculatum* (A. Heller) I. M. Johnst. ex Tidestr.	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
Brassicaceae	*Descurainia pinnata* subsp. *menziesii* (DC.) Detling	Ap	EtOH	NA (HCT-116)	Murillo-Alvarez et al. (2001)
Bromeliaceae	*Aechmea bracteata* var. *bracteata* Griseb.	Lv	BuOH	NA (KB)	Ankli et al. (2002)
	Bromelia pinguin L.	Rt and sm	MeOH	2.1 (KB)	Raffauf et al. (1981)
			$NaHCO_3$	NA (KB)	
Burseraceae	*Bursera bipinnata* (DC.) Engl.	Resin	–	NA (KB), NA (HF-6), 5.2 (MCF-7)	Lautié et al. (2008)
	Bursera copallifera (DC.) Bullock	Sm	Chl	14 (KB), NA (HF-6), 7.1 (MCF-7)	Lautié et al. (2008)
		Fr		NA (KB), NA (HF-6), 5.9 (MCF-7)	
	Bursera graveolens (Kunth) Triana & Planch.	Sm	MeOH	NA (HT-1080)	Nakanishi et al. (2005)
	Bursera fagaroides var. *elongata* McVaugh & Rzed.	Sb	Chl	20 (L5178Y)	Puebla-Pérez et al. (1998), Murillo-Alvarez et al. (2001)
		Ap	EtOH	<0.076 (HCT-116)	
Cactaceae	*Lophophora williamsii*, (Lem. ex Salm-Dyck) J.M. Coult	Tb	MeOH	8.0 (L5178Y-R), 8.1 (U937), NA (L929), 0.18 (MCF-7)	Franco-Molina et al. (2003)
	Pachycereus webery (J. M. Coult.) Backeb.	Ap	PE	NA (HCT-15), NA (KB), NA (UISO)	Popoca et al. (1998)
			EtOAc	NA (HCT-15), NA (KB), NA (UISO)	
			MeOH	NA (HCT-15), NA (KB), NA (UISO)	
Campanulaceae	*Lobelia laxiflora* Kunth	Ap	H_2O	3.2 (KB)	Abbott et al. (1966)
Caprifoliaceae	*Valeriana sorbifolia* Kunth	Ap	Hex	25 (PC-3M)	Xu et al. (2007)
			MeEtAco	25 (PC-3M)	
	Viburnum jucundum C. V. Morton	Ap	Aco	18.2 (UISO), 14.2 (HCT-15), 12.6 (OVCAR-5)	Rios et al. (2001)
Caricaceae	*Carica papaya* L.	Wp	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
Celastraceae	*Crossopetalumgaumeri* (Loes.) Lundell	Lv	DCM	0.7 (KB)	Ankli et al. (2002)
			BuOH	10.2 (KB)	
	Hippocratea excelsa Kunth	Rt	PE	0.76 (HCT-15), 0.004 (KB), 0.006 (UISO)	Popoca et al. (1998)
			EtOAc	2.4 (HCT-15), 4.0 (KB), 3.1 (UISO)	
			MeOH	1.9 (HCT-15), 10.9 (KB), NA (UISO)	
Combretaceae	*Combretum fruticosum* (Loefl.) Stuntz	Ap	H_2O	2.6 (KB)	Abbott et al. (1966)
			EtOH:Chl	NA (KB)	
Commelinaceae	*Tradescantia discolor* L' Hér	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	Mena-Rejon et al. (2009)
		Rb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
	Tradescantia zebrina Bosse var. *zebrina*	Ap	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
Convolvulaceae	*Ipomoea orizabensis* (Pelletan) Ledeb. Ex Steud.	Rt	Chl	2.5 (KB)	Hernández-Carlos et al. (1999)
	Ipomoea pauciflora M. Martens & Galeotti	Sd	EtOH	NA (KB), NA (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	NA (KB), NA (P-388)	
			PE	NA (KB), NA (P-388)	
	Ipomoea wolcottiana subsp. *wolcottiana*	Rt	Chl	4.5 (OVCAR)	León et al. (2006)
Cucurbiataceae	*Ibervillea sonorae* (S. Watson) Greene	Rt	H_2O	4.23 (T-47D), NA (HeLa)	Vega-Avila et al. (2009)
Cupressaceae	*Juniperusdeppeana* Steud.	Bk	EtOH	4.6 (HeLa)	Villavicencio-Nieto et al. (2008)
Ebenaceae	*Diospyros anisandra* S. F. Blake	Lv	DCM	14 (KB)	Ankli et al. (2002)
	Diospyros digyna Jacq.	Rt	MeOH	14 (MCF-7), 13 (H-460), 30 (SF-268)	Calderon et al. (2006)

Table 2 (*Continued*)

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
	Diospyros tetrasperma Sw.	Lv	DCM	NA (KB)	Ankli et al. (2002)
Euphorbiaceae	*Croton reflexifolius* Kunth	Lv	DCM	NA (KB)	Ankli et al. (2002)
	Euphorbia pulcherrima (Willd.) Klotzsch	Ap	H_2O	NA (KB)	Abbott et al. (1966), Villarreal et al. (1992)
		Fw	EtOH	NA (KB), NA (P-388), NA (KB-VI*)	
			Chl	NA (KB), NA (P-388)	
			PE	NA (KB), NA (P-388)	
	Jatropha gaumeri Greenm.	Rt	DCM	7.8 (KB)	Ankli et al. (2002)
			BuOH	NA (KB)	
	Jatropha neopauciflora Pax	Bk	Chl:MeOH	NA (U-251), NA (K-562)	García and Delgado (2006)
Ericaceae	*Comarostaphylis polifolia* (Kunth) Zucc. Ex Klotzsch	Ap	H_2O	3.3 (KB)	Abbott et al. (1966)
			EtOH:Chl	NA (KB)	
Fabaceae	*Acaciella angustissima* (Mill.) Britton & Rose	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	Mena-Rejon et al. (2009)
		Sb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
		Rb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
	Acacia pennatula (Schltdl. & Cham.) Benth.	Bk	PE	NA (HCT-15), 20.9 (KB), 16.6 (UISO)	Popoca et al. (1998)
			EtOAc	NA (HCT-15), 17.4 (KB), 25.1 (UISO)	
			MeOH	NA (HCT-15), NA (KB), 10 (UISO)	
	Albizia occidentalis Brandegee	Ap	H_2O	5.1 (KB)	Abbott et al. (1966)
			EtOH:Chl	NA (KB)	
	Bauhinia divaricata L.	Lv	DCM	NA (KB)	Ankli et al. (2002), Abbott et al. (1966)
		Ap	H_2O	NA (KB)	
	Caesalpinia gaumeri Greenm	Ap	H_2O	8.1 (KB)	Abbott et al. (1966)
	Dalea carthagenensis var. *barbata* (Oerst.) Barneby	Lv	DCM	NA (KB)	Ankli et al. (2002)
	Dialium guianense (Aubl.) Sandwith	Bk	EtOH	6.6 (KB)	Abbott et al. (1966)
			H_2O	NA (KB)	
	Havardia albicans (Kunth) Britton & Rose	Lv	MeOH	28 (MDCK), NA (KB), NA (Hep-2), NA (HeLa), 27 (SiHa)	Mena-Rejon et al. (2009)
		Sb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), 23.5 (SiHa)	
		Rb		NA (MDCK), NA (KB), NA (Hep-2), NA(HeLa), 25 (SiHa)	
	Leucaena leucocephala (Lam.) de Wit subsp. *leucocephala*	Ap	EtOH	2.8 (KB)	Abbott et al. (1966)
	Mimosa tenuiflora (Willd.) Poir.	Sb	EtOH	NA (KB), 18.5 (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	NA (KB), 9.0 (P-388), NA (KB-VI*	
			PE	NA (KB), NA (P-388), NA (KB-VI*	
	Phaseolus acutifolius A. Gray	Sd	Chl:MeOH	NA (HeLa)	García-Gasca et al. (2002)
	Phaseolus vulgaris L.	Sd	MeOH	14.7 (HeLa)	Aparicio-Fernández et al. (2006)
	Piscidia piscipula (L.) Sarg.	Lv	BuOH and DCM	NA (KB)	Ankli et al. (2002)
	Pithecellobium unguis-cati (L.) Benth.	Ap	H_2O	5.0 (KB)	Abbott et al. (1966)
			EtOH:Chl	2.2 (KB)	
	Senna occidentalis (L.) H. S. Irwin & Barneby	Lv	EtOH	4.2 (MCF-7), 5.4 (H-460), 3.9 (SF-268)	Calderon et al. (2006)
	Senna racemosa (Mill) H.S. Irwin & Barneby	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), 28 (SiHa)	Mena-Rejon et al. (2009)
		Sb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
		Rb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
	Vachellia campechiana (Mill.) Seigler & Ebinger	Ap	EtOH	3.7 (KB)	Abbott et al. (1966)
Hypericaceae	*Hypericum silenoides* Juss. subsp. *silenoides*	Lv	EtOH	9.8 (MCF-7), NA (H-460), 6.4 (SF-268)	Calderon et al. (2006)
			Chl	3.2 (MCF-7), 5.5 (H-460), 7.2 (SF-268)	
Krameriaceae	*Krameria pauciflora* DC.	Ap	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
Lamiaceae	*Hyptis pectinata* (L) Poit	Ap	Chl	2.2 (P-388)	Pereda-Miranda et al. (1993)
	Hyptis suaveolens (L.) Poit	Rt	Chl	12.3(KB), 12.7 (HF-6), 0.8 (MCF-7)	Lautié et al. (2008)
		Sm		NA (KB), 9.9 (HF-6), 5.2 (MCF-7)	
		Lv		NA (KB), 14.9 (HF-6), 4 (MCF-7)	
	Hyptis verticillata Jacq.	Ap	Hex:Chl	0.3 (P-388)	Novelo et al. (1993)
Lauraceae	*Persea americana* Mill	Ft	EtOH:CHl	NA (A-549), NA (MCF-7), NA (HT-29), 6.9 (A-498), 3.1 (PC-3), NA (PaCa-2)	Oberlies et al. (1998)
Linaceae	*Linum scabrellum* Planch.	Rt	Chl	0.2 (KB), 0.2 (HF-6), 4.8 (MCF-7)	Lautié et al. (2008)
		Ap		0.2 (KB), 0.2 (HF-6), 4.8 (MCF-7)	
		Rt	BuOH	0.2 (KB), 0.2 (HF-6), 4.8 (MCF-7)	
Lythraceae	*Cuphea aequipetala* Cav.	Wp	Aco-H_2O	NA (Hep-2), 18.7 (HCT-15), 8.1 (DU-145)	Vega-Avila et al. (2004), Waizel-Bucay et al. (2003), Villarreal et al. (1992)

Table 2 (*Continued*)

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
		Ap	MeOH	NA (KB), 17.4 (UISO), NA (COLADCAR), NA (HCT-15)	
			EtOAc	NA (KB), NA (UISO), NA (COLADCAR), NA (HCT-15)	
			HEX	NA (KB), NA (UISO), NA (COLADCAR), NA (HCT-15)	
		Lv	EtOH	NA (KB), 18.5 (P-388), NA (KB-VI*)	
			Chl	NA (KB), 9.0 (P-388), NA (KB-VI*)	
			PE	NA (KB), NA (P-388), NA (KB-VI*)	
Loranthaceae	*Cladocolea grahamii* (Benth.) Tieg.	Sm	MeOH	NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	Waizel-Bucay et al. (1994)
		lv		NA (OVCAR), NA (KB), 3.0 (P-388), NA (UISO), NA (HCT-15)	
		lf		NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	
		Sm	Hex	10.0 (OVCAR), 5.0 (KB), 3.0 (P-388), NA (UISO), NA (HCT-15)	
		lv		NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	
		lf		1.0 (OVCAR), NA (KB), 1.8 (P-388), NA (UISO), NA (HCT-15)	
	Psittacanthus calyculatus (DC.) G. Don	Ap	EtOH	27.8 (KB), NA (Caco-2)	Frei et al. (1998)
Malpighiaceae	*Galphimia glauca* Cav.	Lv	EtOH	NA (KB), NA (UISO), NA (OVCAR-5), 0.63 (COLON)	Aguilar-Santamaría et al. (2007), Camacho et al. (2003)
			MeOH	NA (KB), NA (UISO), NA (OVCAR-5), 0.5 (COLON)	
			H_2O	NA (KB), NA (UISO), NA (OVCAR-5), 1.99 (COLON)	
		ap	MeOH	NA (KB)	
			H_2O	NA (KB)	
Malvaceae	*Gossypium hirsutum* L.	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	Mena-Rejon et al. (2009)
		Sb		NA (MDCK), NA (KB), NA (Hep-2), 20 (HeLa), NA (SiHa)	
		Rb		NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
	Luehea alternifolia (Mill.) Mabb.	Lv	BuOH	NA (KB)	Ankli et al. (2002)
Meliaceae	*Swietenia humilis* Zucc.	Bk	MeOH	11.48 (KB)	Camacho et al. (2003)
	Swietenia macrophylla King	Bk	MeOH	NA (KB)	Camacho et al. (2003)
		Lv		24 (KB)	
Moraceae	*Dorstenia contrajerva* L.	Rh	BuOH and DCM	NA (KB)	Ankli et al. (2002)
	Dorstenia drakena L.	Rt	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
Myrtaceae	*Psidium guajava* L.	Ap	H_2O	3.8 (KB)	Abbott et al. (1966), Villarreal et al. (1992)
			EtOH	NA (KB), 7.6 (P-388), NA (KB-VI*)	
			Chl	7.9 (KB), 12.0 (P-388), NA (KB-VI*)	
			PE	10.0 (KB), 12.5 (P-388), NA (KB-VI*)	
	Psidium sartorianum (O. Berg) Krug & Urb.	Lv	BuOH and DCM	NA (KB)	Ankli et al. (2002)
Orchidaceae	*Stenorrhynchos lanceolatus* (Aubl.) L. C. Rich.	Ap	MeOH	NA (KB)	Camacho et al. (2003)
			H_2O	NA (KB)	
	Vanilla planifolia Andrews	Rt	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
Papavaraceae	*Bocconia frutescens* L.	Lv	EtOH	NA (MCF-7), NA (H-460), NA (SF-268)	Calderon et al. (2006)
Phytolaccaceae	*Petiveria alliacea* L.	Lv	H_2O	NA (U-251), NA (PC-3), NA (K-562), NA (HCT-15), NA (MCF-7)	Perez-Leal et al. (2006), Calderon et al. (2006)
			EtOH	22 (MCF-7), 22 (H-460), NA (SF-268)	
Picramniaceae	*Alvaradoaamorphoides* Liebm.	Lv	DCM	10 (KB)	Ankli et al. (2002)
			BuOH	14 (KB)	
	Castela tortuosa Liebm.	Wp	EtOH	8.7 (KB), 0.002 (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	NA (KB), NT (P-388), NA (KB-VI*)	
			PE	NA (KB), NA (KB-VI*)	
	Picramnia antidesma subsp. *fessonia* (DC.) W. W. Thomas	Rb	Et_2O	9.7×10^{-4} (KB)	Hernández-Medel and Pereda-Miranda (2002)
			MeOH	>0.02 (KB)	
Picrodendraceae	*Piranhea mexicana* (Standl.) Radcl.-Sm.	Lv	MeOH	NA (KB)	Camacho et al. (2003)
			H_2O	NA (KB)	
Pinaceae	*Pinus patula* Schltdl. & Cham.	Bk	H_2O	4.1 (KB)	Abbott et al. (1966)
		Ap		NA (KB)	
Piperaceae	*Piper aduncum* L.	Lv	EtOH	27 (MCF-7), 25 (H-460), 23 (SF-268)	Calderon et al. (2006)
Plumbaginaceae	*Plumbago pulchella* Boiss.	Ap	EtOH	NA (KB), NA (P-388)	Villarreal et al. (1992)
			Chl	NA (KB), NA (P-388)	
			PE	NA (P-388)	
			EtOH	NA (KB-VI*)	
			Chl	NA (KB-VI*)	
			PE	NA (KB), 12.5 (P-388)	
		Rt	EtOH	19 (KB), 2.5 (P-388)	

Table 2 (*Continued*)

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
			Chl	NA (KB), NA (P-388)	
Poaceae	*Zea mays* L	Wp	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
Polypodiaceae	*Microgramma nitida* (J. Sm.) A. R. Sm.	Wp	BuOH	NA (KB)	Ankli et al. (2002)
Primulaceae	*Bonellia macrocarpa* subsp. *pungens* (A. Gray) B. Stahl & Källersjô	Ap	H_2O	NA (KB)	Abbott et al. (1966), Del Amo (1979)
			EtOH:Chl	5 (KB)	
Rhamnaceae	*Colubrina macrocarpa* (Cav.) G. Don	Rt	PE	10 (HCT-15), 6.6 (KB), NA (UISO)	Popoca et al. (1998)
			EtOAc	2.1 (HCT-15), 5.8×10^{-6} (KB), 0.6 (UISO)	
			MeOH	9.1 (HCT-15), 6.3×10^{-4} (KB), 0.08 (UISO)	
Rizhophoraceae	*Rhizophora mangle* L.	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), 16 (HeLa), 18 (SiHa)	Mena-Rejon et al. (2009)
		sb		NA (MDCK), NA (KB), NA (Hep-2), 17 (HeLa), 22 (SiHa)	
		rb		NA (MDCK), NA (KB), NA (Hep-2), 16 (HeLa), 21 (SiHa)	
Rubiacaeae	*Hamelia patens* Jacq.	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	Mena-Rejon et al. (2009)
		Sb	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	
		Rb	MeOH	NA (MDCK), NA (KB), NA (Hep-2), 13 (HeLa), 22 (SiHa)	
	Hintonia latiflora (Sessé & Moc. Ex DC.) Bullock	Sb	EtOAc	NA (KB), NA (P388), NA (UISO)	Argotte-Ramos et al. (2006), Camacho et al. (2003)
			MeOH	NA (KB)	
		Bk	H_2O	NA (KB)	
	Morinda royoc L.	Ft	DCM	NA (KB)	Ankli et al. (2002)
	Nernstia mexicana (Zucc. & Mart. ex DC.) Urb.	Ap	MeOH	13.04 (KB)	Camacho et al. (2003)
Rutaceae	*Casimiroa tetrameria* Millsp.	Lv	DCM	NA (KB)	Ankli et al. (2002)
Salicaceae	*Casearia nitida* (L.) Jacq	Lv	DCM	NA (KB)	Ankli et al. (2002)
Sapotaceae	*Chrysophyllum mexicanum* Brandegee ex Standl.	Rt	BuOH	NA (KB)	Ankli et al. (2002)
	Manilkara zapota (L.) Van Royen	Ft	MeOH	NA (HCT-116), NA (SW-480)	Ma et al. (2003)
Smilacaceae	*Smilax aristolochiifolia* Mill.	Rt	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
Solanaceae	*Capsicum annum* L.	Lv	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)
	Cestrum nocturnum L.	Lv	EtOH	21 (MCF-7), 15 (H-460), 20 (SF-268)	Calderon et al. (2006)
	Solanum chrysotrichum Schltdl.	Lv	EtOH	NA (KB), NA (P-388), NA (KB-VI*)	Villarreal et al. (1992)
			Chl	NA (KB), NA (P-388), NA (KB-VI*)	
			PE	NA (KB), NA (P-388), NA (KB-VI*)	
	Solanum lanceolatum Cav.	Lv	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
	Solanumrostratum Dun.	Br	EtOH	NA (HeLa)	Villavicencio-Nieto et al. (2008)
Verbenaceae	*Citharexylum ellipticum* D. Don	Ap	H_2O	6.2 (KB)	Abbott et al. (1966)
	Lantana involucrata L.	Ap	H_2O	4.1 (KB)	Abbott et al. (1966)
			EtOH:Chl	5 (KB)	
	Lantana urticifolia Mill.	Ap	H_2O	5.0 (KB)	Abbott et al. (1966)
Viscaceae	*Phoradendron carneum* Urb.	Ap	EtOH	NA (KB), NA (Caco-2)	Frei et al. (1998)
	Phoradendron galeottii Trel.	Sm	MeOH	NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	Waizel-Bucay et al. (1994)
		lv		NA (OVCAR), NA (KB), 3.0 (P-388), NA (UISO), NA (HCT-15)	
		lf		NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	
		Sm	Hex	9.0 (OVCAR), NA (KB), NA (P-388), 8.0 (UISO), NA (HCT-15)	
		lv		NA (OVCAR), NA (KB), 5.0 (P-388), NA (UISO), NA (HCT-15)	
		lf		NA (OVCAR), NA (KB), 10.0 (P-388), NA (UISO), NA (HCT-15)	
	Phoradendron reichenbachianum (Seem.) Oliver	Sm	MeOH	NA (OVCAR), NA (KB), 3.0 (P-388), NA (UISO), NA (HCT-15)	Waizel-Bucay et al. (1994)
		lv		NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	
		lf		NA (OVCAR), NA (KB), NA (P-388), NA (UISO), NA (HCT-15)	
		Sm	Hex	NA (OVCAR), NA (KB), 3.0 (P-388), NA (UISO), NA (HCT-15)	
		lv		NA (OVCAR), NA (KB), 5.0 (P-388), NA (UISO), NA (HCT-15)	
		lf		1.0 (OVCAR), NA (KB), 1.5 (P-388), NA (UISO), NA (HCT-15)	

Table 2 (*Continued*)

Family	Scientific name	Plant part	Extract	ED_{50} μg/ml (cell line)	Reference
Zamiaceae	*Dioon spinulosum* Dyer ex Eichl	Lv	MeOH	NA (MDCK), NA (KB), NA (Hep-2), NA (HeLa), NA (SiHa)	Mena-Rejon et al. (2009)
		Pt		NA (MDCK), NA (KB), 20 (Hep-2), NA (HeLa), NA (SiHa)	
Zygophyllaceae	*Larrea tridentata* (DC.) Cav.	Wp	EtOH	NA (Neuro-2A)	Mazzio and Soliman (2009)

Nature of the extracts: BuOH, butanol; Chl, chloroform; DCM, dichloromethane; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexane; H_2O, aqueous; MeOH, methanol; MeEtAco, methy ethyl acetone; PE, petroleum ether; Aco, acetone; Et_2O dy ethyl ether.
Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Tb, tubercle; Wp, whole plant.
Cell lines: 1301, lymphoblastic leukemia; A-498, human kidney carcinoma; A-549, human lung carcinoma; Caco-2, human epithelial colorectal adenocarcinoma; COLON, colon carcinoma; DU-145, prostate carcinoma; H-460, human large cell lung carcinoma; HCT-15 COLADCAR, adherent colon carcinoma; HCT-116, human colorectal carcinoma; HeLa, cervix adenocarcinoma; Hep-2, laryngeal carcinoma, HepG2, hepatocarcinoma; HF-6, human colon carcinoma; HT-29, human colon adenocarcinoma; HT1080, human fibrosarcoma; K-562, chronic myeloblastic leukemia, KB, human nasopharynx carcinoma; L5178Y-R, murine lymphoma; L929, mouse fibroblasts; MDCK, canine kidney cells, MCF-7, human breast carcinoma; Neuro-2a, mouse neuroblastoma, P-388, mouse leukemia; PACA-2, human pancreatic carcinoma; PC-3, human prostate adenocarcinoma; SF268, glioma; SW-480, colon adenocarcinoma; T47D, breast cancer; U251, human glioma; U937, human leukemic monocyte lymphoma, UISO-SQC-1, squamous cervix carcinoma; OVCAR, ovary carcinoma; SiHa, cervix squamous carcinoma.
VI*, denotes drug resistance.

have been studied *in vitro* and *in vivo* (Tables 1–6). Another 119 plants were recorded which are used for empirical treatment of diseases with cancer symptomatology without scientific studies (Table 7). The botanical correct names were corroborated at Missouri Botanical Garden-Tropicos (2010) and International Plant Names Index (2008). In some cases the plant names were updated on their taxonomy and nomenclature.

From plants with scientific reports (181), only 114 of these are employed for the empirical treatment of cancer (Table 1), whereas ethnobotanical knowledge for cancer treatment is lacking for 67 of these (Table 1). Plants in the last group are used popularly to treat some other diseases, and all of them have also been subjected to laboratory evaluations including cytotoxic analysis.

From those plants with empirical knowledge for cancer treatment (Table 1A), 75 present active effects, whereas the remaining 39 lack activity. On the other hand, from plants with no traditional knowledge for cancer treatment (Table 1B), 33 present activity and 34 lack effects. The criteria to indicate activity refers to plants from which their extracts and/or isolated compounds have shown *in vitro* or *in vivo* effects according to Suffness and Pezzuto (1990).

Considering only data of Table 1A in which 73% of the listed plants were active, ethnobotanical information appears to contribute for the selection of candidates; but when reviewing those data presented in Table 1B in which up to 49% of the plants (not used to treat conditions consistent with cancer symptomatology) were active, it appears that folklore tradition might not be precisely a good basis for the selection of candidates. In addition, it is important to underline that less than 10% of the plants included in Tables 1A and 1B were subjected to *in vivo* studies and, as pointed in Section 5, many of the plants showing cytotoxicity could be eliminated as potential candidates when assayed in animal models. It is also interesting to point out that many of the plants in Table 1B are empirically employed for dermatological and inflammatory conditions.

The ethnomedical categories proposed by Heinrich et al. (1998) were used in this review (see Tables 1 and 7). Gatrointestinal disorders include vomiting, diarrhea, stomach ache, dysentery, gastritis, peptic, and gastric ulcers. Respiratory illnesses refer to cough, tuberculosis, pneumonia, cold, flu and asthma. Inflammatory diseases consist of wounds and rheumatism. Dermatological diseases include prevention of hair loss, itch, skin ulcers, abscesses, cicatrization, burns, wart, bruises and injuries caused by venomous creatures. Venereal diseases refer to gonorrhea, syphilis and other diseases. Gynecological disorders include vaginal infections, ovarian and uterine cancer. Urological problems refer to kidney stones, diabetes, kidney and bladder infections. Finally, neurological disorders include anxiety and epilepsy.

5. Plant extracts with *in vitro* and in *vivo* studies

Of those plant extracts with cytotoxic studies (Tables 1A and 1B), only 88 (56%) have demonstrated active effects in at least one cancer cell line (Table 2). However, this number might be overestimated since, in general, negative results are published only if a screening of cytotoxic effects of many plants extract is carried out, and thus plant extracts without active cytotoxic effects are not reported. Fourteen plant extracts with active cytotoxic effects have been tested *in vivo*. Although there is not a criterion to indicate that a plant extract presents active anti-tumor effects, tumor inhibitory growth and survival time are the most common strategies to evaluate anti-tumor action. From extracts presented in Table 3, only the aqueous extract of *Albizia occidentalis* aerial parts induced 49% tumor inhibitory growth in Swiss mice bearing sarcoma 180 cells at doses less than 100 mg/kg. The rest of the extracts induce, in some cases, tumor inhibitory growth higher than 50% but tested at doses above 100 mg/kg (Table 3). Toxicity *in vitro* does not necessarily translate to *in vivo* activity. This situation has been explained by the fact that the active principles of an extract could be metabolized and/or detoxified in the animal, and in consequence looses the possible antineoplasic effects.

Chemotaxonomic studies might provide an alternative way to find active compounds. As an example, McKee et al. (1998) analyzed 315 organic extracts from 31 taxa of *Calophyllum* genus to obtain related pyranocoumarins, a class of nonnucleoside specific inhibitors of HIV-1 reverse transcriptase. Of the analyzed extracts, 25% were identified as positive for pyranocoumarins.

In our study, the botanical families with the highest number of plant species that have shown antineoplasic effects *in vitro* and *in vivo* are: Asteraceae (34), Fabaceae (19), Lamiaceae (7) and Convolvulaceae (6). Although the Asteraceae family possesses the highest number of plant extracts studied experimentally, only *Gymnosperma glutinosum*, *Helianthella quinquenervis*, *Heterotheca inuloides*, *Melampodium paniculatum*, *Montanoa leucantha*, *Smallanthus maculatus*, *Verbesina persicifolia* and *Viguiera decurren*, have been shown to exert active cytotoxic effects (Table 2).

6. Compounds with *in vitro* and *in vivo* studies

The isolation of active compounds is a crucial step for finding new anti-cancer drugs. Many Mexican plant extracts with active cytotoxic effects have been studied and a great variety of compounds (terpenes, glycosides, lignans, acetogenins) have been isolated (Tables 4–6). A total of 187 compounds, belonging to 19 types of plant secondary metabolites, have been isolated from 51 plant extracts with active cytotoxic effects, and of

Table 3
Anti-tumor effects of Mexican plant extracts.

Family	Scientific name	Plant part	Extract	Animal system	Dose (mg/kg)	Route of administration	Time (days)	Tumor system (tumor inhibition, %)	Reference
Asteraceae	*Gymnosperma glutinosum* (Spreng.) Less.	Lv	Hex	BALB/c mice BALB/c mice	5 0.5	It Iv	19	DBA/2 lymphoma (20) DBA/2 lymphoma (31)	Gomez-Flores et al. (2009)
Betulaceae	*Alnus jorullensis* Kunth subsp. *jorulensis*	Ap	H_2O	Swiss mice BDF1 mice Syrian hamsters	175 250 175	Ip Ip Ip	6	Sarcoma 180 (18) Lymphoid leukemia 1210 (NA) Adenocarcinoma of the duodenum (58)	Abbott et al. (1966)
Bixaceae	*Cochlospermum vitifolium* (Willd.) Spreng.	Ft	H_2O	Swiss mice BDF1 mice BDF1 mice	140 112 112	Ip Ip Ip	8	Sarcoma 180 (12) Lymphoid leukemia 1210 (NA) Solid friend virus leukemia (46)	Abbott et al. (1966)
Combretaceae	*Combretum fruticosum* (Loefl.) Stuntz	Ft	H_2O	Swiss mice BDF1 mice BDF1 mice	70 112 112	Ip Ip Ip	8	Sarcoma 180 (45) Lymphoid leukemia 1210 (NA) Solid friend virus leukemia (57)	Abbott et al. (1966)
Fabaceae	*Acacia millenaria* Standl.	Ap	EtOH	Swiss mice BDF1 mice BDF1 mice	125 57 113	Ip Ip Ip	8	Sarcoma 180 (NA) Adenocarcinoma 755 (43) Lymphoid leukemia 1210 (NA)	Abbott et al. (1966)
	Albizia occidentalis Brandegee	Ap	H_2O	Swiss mice BDF1 mice Syrian hamsters	25 8.0 18	Ip Ip Ip	8	Sarcoma 180 (49) Lymphoid leukemia 1210 (NA) Adenocarcinoma of the duodenum (6)	Abbott et al. (1966)
	Caesalphinia gaumeri Greenm.	Ap	H_2O	Swiss mice BDF1 mice BDF1 mice	125 100 25	Ip Ip Ip	8	Sarcoma 180 (50) Adenocarcinoma 755 (27) Lymphoid leukemia 1210 (NA)	Abbott et al. (1966)
Lamiaceae	*Hyptis emory* Torr.	Ap	Chl	Sprague rats	400 600	Im Im	15	Walker carcinoma 5WA16 (53) Walker carcinoma 5WA16 (64)	Sheth et al. (1972)
Pinaceae	*Pinus patula* Schltdl. & Cham.	Bk	H_2O	Swiss mice BDF1 mice BDF1 mice	32 26 26	Ip Ip Ip	8	Sarcoma 180 (13) Lymphoid leukemia 1210 (NA) Solid friend virus leukemia (46)	Abbott et al., 1966
Verbenaceae	*Citharexylum ellipticum* D. Don	Ap	H_2O	Swiss mice BDF1 mice Syrian hamster	250 200 200	Ip Ip Ip	8	Sarcoma 180 (53) Solid friend virus leukemia (33) Adenocarcinoma of the duodenum (59)	Abbott et al., 1966
	Lantana involucrata L.	Ap	EtOH:Chl	Swiss mice BDF1 mice BDF1 mice	125 100 100	Ip Ip Ip	8	Sarcoma 180 (43) Lymphoid leukemia 1210 (NA) Solid friend virus leukemia (44)	Abbott et al. (1966)
	Lantana urticifolia Mill.	Ap	H_2O	Swiss mice BDF1 mice Syrian hamsters	125 100 100	Ip Ip Ip	8	Sarcoma 180 (23) Solid friend virus leukemia (4) Adenocarcinoma of the duodenum (60)	Abbott et al. (1966)

Nature of the extracts: BuOH, buthanol; Chl, chloroform; DCM, dichloromethane; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexane; H_2O, aqueous; MeOH, methanol; MeEtAco, methy ethyl acetone; PE, petroleum ether; Aco, acetone; Et_2O, dy ethyl ether.
Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Wp, whole plant.
Route of administration: Im, intramuscular; Ip, intraperitoneal; It, intratumoral; Iv, intravenous.

Table 4
Cytotoxicity of pure compounds isolated from Mexican plant species.

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
Agavaceae	*Agave americana* L.	Lv	BuOH	Hecogenin tetraglycoside	Saponin	NA (HL-60)	Yokosuka et al. (2000)
Anacardiaceae	*Amphipterygium adstringens* (Schltdl.) Standl.	Bk	Hex	Masticadienonic acid	Terpene	NA (HCT-15), NA (MCF-7), NA (U-251), NA (PC-3), NA (K-562)	Oviedo-Chávez et al. (2004)
				3-α-hydroxymasticadienolic acid	Terpene	NA (HCT-15), NA (MCF-7), NA (U-251), NA (PC-3), NA (K-562)	
Annonaceae	*Annona diversifolia* Saff.	Sd	Hex	Laherradurin	Acetogenin	0.015 (HeLa), 0.015 (SW-480)	Schlie-Guzmán et al. (2009)
				Cherimolin-2	Acetogenin	0.05 (HeLa), 0.5 (SW-480)	
	Mosannona depressa (Baill.) Chatrou	Sb	Chl	1,2,3,4-Tetramethoxy-5-(2-propenyl)benzene	Glycoside	NA (A-549), NA (MCF-7), NA (HT-29)	Jimenez-Arellanes et al. (1996)
	Rollinia mucosa (Jacq.) Baill.	Lv sd	EtOH:CHl	Rollinecin A	Acetogenin	1.14×10^{-4} (A-549), 1.44 (MCF-7), 1.6 (HT-29), 7.25×10^{-4} (A-498), 2.62×10^{-4} (PC-3), 3.47×10^{-5} (PACA-2)	Shi et al. (1997), Chávez et al. (1998), Chávez et al. (1999)
				Rollinecin B	Acetogenin	4.2×10^{-4}(A-549), 2.72 (MCF-7), 1.44 (HT-29), 2.29×10^{-4} (A-498), 3.62×10^{-4} (PC-3), 2.53×10^{-4} (PACA-2)	
				Rollitacin	Acetogenin	NA (A-549), 0.25 (MCF-7), NA(HT-29), NA (A-498), NA (PC-3), NA (PACA-2)	
				Rollinacin	Acetogenin	NA (A-549), NA (MCF-7), NA (HT-29), NA (A-498), 2500 (PC-3), NA (PACA-2)	
				Jimenezin	Acetogenin	0.016 (A-549), NA (MCF-7), 4.25×10^{-3} (HT-29), 4.94×10^{-2} (A-498), 2.77×10^{-4} (PC-3), 1.69×10^{-4} (PACA-2)	
				Membranacin	Acetogenin	0.4 (A-549), 2.18 (MCF-7), 3.04 (HT-29), $<10^{-3}$ (A-498), $<10^{-3}$ (PC-3), 2.10 (PACA-2)	
				Desacetyluvaricin	Acetogenin	0.47 (A-549), 1.35 (MCF-7), 1.69 (HT-29), $<10^{-3}$ (A-498), $<10^{-3}$ (PC-3), 1.92 (PACA-2)	
	Helianthella quinquenenervis (Hook) A. Gray	Rt	MeOH	6-Methoxytremetone	Benzofuran	NA (MCF-7), NA (HT-29), 1 (A-549)	Castañeda et al. (1996)
				6-Hydroxy-3-methoxytremetone	Benzofuran	NA (MCF-7), NA (HT-29), NA (A-549)	
				4-β-D-(Glucopyranosyloxy)-3-(3-methoxy-*trans*-isopenten-1-yl]acetophenone	Glycoside	NA (MCF-7), NA (HT-29), NA (A-549)	
				Demethylencecalin	Chromene	2 (MCF-7), 2 (HT-29), NA (A-549)	
				Euparin	Benzofuran	NA (MCF-7), NA (HT-29), NA (A-549)	
				Encecalin	Chromene	NA (MCF-7), NA (HT-29), NA (A-549)	
	Iostephane heterophylla (Cav.) Benth. ex Hemsl.	Roots	Chl	Xanthorrihizol	Terpene	NA (KB), NA (UISO), NA (HCT-15)	Aguilar et al. (2001)
				Trachylobanoic acid	Terpene	1.0 (UISO)	
	Parthenium argentatum Gray	Resin		Argentatin A	terpene	NA (U-251), NA (PC-3), NA (HCT-15), NA (MCF-7), NA (K-562)	Parra-Delgado et al. (2005)
				Argentatin B	Terpene	NA (U-251), NA (PC-3), NA (HCT-15), NA (MCF-7), NA (K-562)	
	Pseudognaphalium semiamplexicaule (DC.) Anderb.	Lv	Hex	Gnaphaliin	Flavonoid	NA (LLC-MK2), NA (C6)	Sanchez et al. (2001)

Table 4 (*Continued*)

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
	Roldana angulifolia (D.C.)H. Rob. &Brettell	Rt	Hex:Aco	Angulifolide	Terpene	NA (U-251), NA (PC-3), NA (K-562), NA (HCT-15), NA (MCF-7), NA (SKLU-1)	Arciniegas et al. (2006)
				13-Acetoxy-14-oxocacalohastin	Terpene	NA (U-251), NA (PC-3), NA (K-562), NA (HCT-15), NA (MCF-7), NA (SKLU-1)	
				13-hydroxy-14-oxocacalohastin	Terpene	NA (U-251), NA (PC-3), NA (K-562), NA (HCT-15), NA (MCF-7), NA (SKLU-1)	
	Roldana sessilifolia (Hook. & Am.) H. Rob. & Brettel	Rt	Hex	1α-angeloyloxy-10βH, 8β hydroxy-eremophyl-7(11)-en-8α, 12-olide	Terpene	NA (KB), NA (P-388), NA (KB-VI*)	Villarreal et al. (199)4
				1α-Angeloyloxy-10β hydroxy-eremophyl-7(11)-en-8α, 12-olide	Terpene	NA (KB), NA (P-388), NA (KB-VI*)	
				1α-Angeloyloxy-10βH, 8β hydroxy-eremophyl-7(11)-en-8α, 12-olide	Terpene	NA (KB), NA (P-388), NA (KB-VI*)	
	Schkuhria schkuhrioides Thell.	Ap	Hex	Frutescin	Terpene	NA (KB), NA (UISO), NA (COLON)	Delgado et al. (1998)
				Schkuhriolide	Terpene	NA (KB), NA (UISO), NA (COLON)	
				Frutescinic acid	Terpene	NA (KB), NA (UISO), NA (COLON)	
				allo-schkuhriolide	Terpene	5.7×10^{-4} (KB), 1.82 (UISO), 0.9 (COLON)	
				Epoxyschkuhriolide	Terpene	NA (KB), NA (UISO), NA (COLON)	
	Smallanthus maculatus (Cav.) H. Rob.	Ap	Aco	Ursolic acid	Terpene	3.7 (HCT-15), 3.4 (UISO), 3.6 (OVCAR-5)	Rios and León (2006)
	Viguiera decurrens (A. Gray)	Rt	Hex: EtOAc:MeOH	β-D-glucopyranosyl-oleanolate	Saponin	NA (KB), NA (P-388), NA (OVCAR), NA (COLON), NA (UISO)	Marquina et al. (2001)
				Oleanolic acid-3-*O*-methyl-β-D-glucuronopyranosiduronoate	Saponin	NA (KB), NA (P-388), NA (OVCAR), NA (COLON), NA (UISO)	
	Viguiera lactibracteata (Hemsl.) Blake	Ap	Chl:Aco	Niveusin-C	Terpene	2.7 (KB), 0.01 (P-388), NA (KB-VI*)	Villarreal et al. (1994)
	Viguiera quinqueradiata|(Cav.) A. Gray	Lv	Chl	Budlein A	Terpene	1.0 (KB), 1.0 (P-388), NA (KB-VI*)	Villarreal et al. (1994)
Bignoniaceae	*Astianthus viminalis* (Kunth) Baill.	Lv	MeOH	Campenoside	Glycoside	NA (P-388), NA (KB)	Alvarez et al. (1994)
				5-Hydroxycampenoside	Glycoside	NA (P-388), NA (KB)	
	Tecoma stans (L.) Juss. ex Kunth	Fw and fr	EtOH	4-*O*-E-caffeoyl-α-l-rhamnopyranosyl-(1 → 3)-α/β-D-glucopyranose	Glycoside	NA (Hep-G2), NA (MCF-7), NA (1301)	Marzouk et al. (2006)
				E/*Z*-acetoside	Glycoside	NA (Hep-G2), NA (MCF-7), NA (1301)	
				Isoacetoside	Glycoside	NA (Hep-G2), NA (MCF-7), NA (1301)	
				5-Hydroxy-skytanthine hydrochloride	Alkaloid	NA (Hep-G2), NA (MCF-7), NA (1301)	
Burseraceae	*Bursera graveolens* (Kunth) Triana & Planch.	sm	MeOH	Burseranin	Lignan	NA (HT-1080)	Nakanishi et al. (2005)
				Picropolygamain	Lignan	1.9 (HT-1080)	

				Epi-lupeol	Terpene	NA (HT-1080)	
				Lupeol	Terpene	NA (HT-1080)	
	Bursera grandifolia (Schltdl.) Engl.	sb	MeOH	Deoxypodophyllotoxin	Lignan	2×10^{-4} (A-431), 0.03 (BC-1), 3×10^{-2} (Col-2), 0.01 (HT), <0.16 (KB), <0.16 (KB-V1*), 3×10^{-2} (LNCaP), 3×10^{-2} (Lu1), NA (Mel2), 0.06 (U373), 3×10^{-2} (ZR-75-1), 0.16 (ASK)	Wickramaratne et al. (1995)
				β-Peltatin methyl ether	Lignan	0.01 (A-431), 0.05 (BC-1), 2×10^{-3} (Col-2), 0.01 (HT), <0.16 (KB), <0.16 (KB-V1*), 5×10^{-3} (LNCaP), 4×10^{-3} (Lu1), NA (Mel2), 3.10 (U373), 0.01 (ZR-75-1), 0.16 (ASK)	
				Picro-β-peltatin methyl ether	Lignan	0.2 (A-431), NA (BC-1), NA (Col-2), 3.9 (HT), 0.5 (KB), NT (KB-V1*), 0.6 (LNCaP), 0.2 (Lu1), NA (Mel2), 0.7 (U373), NA (ZR-75-1), NA (ASK)	
				Dehydro-β-peltatin methyl ether	Lignan	NA (A-431), 2.9 (BC-1), 3.2 (Col-2), 3.4 (HT), 2.2 (KB), NA (KB-V1*), 3.2 (LNCaP), NA (Lu1), NT (Mel2), NA (U373), NA (ZR-75-1), NA (ASK)	
Capparidaceae	*Polanisia dodecandra* (L.) DC.	Wp	MeOH	5,3′-dihydroxy-3,6,7,8,4′-pentamethoxyflavone	Flavonoid	0.04 (KB), 0.6 (A-459), NA (HCT-8), 0.05 (P-388), 0.55 (PRMI-7591), 0.07 (TE-671)	Shi et al. (1995)
				5,4′-Dihydroxy-3,6,7,8,3′-pentamethoxyflavone	Flavonoid	NA (KB), NA (A-459), NA (HCT-8), NA (P-388), NA (PRMI-7591), 0.98 (TE-671)	
Celastraceae	*Hippocratea excelsa* Kunth	Rt and Sb	Hex: MeOH	Hippocrateine I	Alkaloid	NA (A-549), NA (HT-29), NA (MCF-7)	Mata et al. (1990)
Convolvulaceae	*Ipomoea wolcottiana* subsp. *wolcottiana*	Rt	Hex:DCM	Arboresin 1	Glycoside	NA (HCT-15), NA (UISO), NA (OVCAR-5)	León et al. (2006)
				Arboresin 2	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Arboresin 3	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Arboresin 4	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Arboresin 5	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Arboresin 6	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Murucin 6	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Murucin 7	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Murucin 8	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
				Murucin 9	Glycoside	NA (HCT-15), NA (UISO),NA (OVCAR-5)	
	Ipomoea murucoides Roem. et Schult.	Fw	Chl	Murucoidin I	Glycoside	NA (KB), NA (Hep-2)	Chérigo and Pereda-Miranda (2006)
				Murucoidin II	Glycoside	NA (KB), NA (Hep-2)	
				Murucoidin III	Glycoside	NA (KB), NA (Hep-2)	
				Murucoidin IV	Glycoside	4 (KB), 4 (Hep-2)	
				Murucoidin V	Glycoside	NA (KB), NA (Hep-2)	
				Stoloniferin I	Glycoside	NA (KB), NA (Hep-2)	
	Ipomoea orizabensis (Pelletan) Ledeb. Ex Steud.	Rt	Hex:Chl	Scammonin I	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	Hernández-Carlos et al. (1999), León-Rivera et al. (2008)
				Scammonin II	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Orizabin V	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	

Table 4 (*Continued*)

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
				Orizabin VI	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Orizabin VII	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Orizabin VIII	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Tyrianthinic acid I	Glycoside	2.6 (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Tyrianthinic acid II	Glycoside	2.8 (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Tyrianthin 8	Glycoside	2.2 (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Tyrianthin 9	Glycoside	2.5 (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
	Ipomoea pes-caprae (L.) R. Br.	Wp	Hex	Pescaproside A	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	Pereda-Miranda et al. (2005)
				Pescaprein I	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Pescaprein II	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Pescaprein III	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Pescaprein IV	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
				Stoloniferin III	Glycoside	NA (KB), NA (UISO), NA (HCT-15), NA (OVCAR)	
	Ipomoea stans Cav.	Rt	Hex	Stansin 1	Glycoside	NA (UISO), NA (HCT-15), NA (OVCAR)	León et al. (2004)
				Stansin 2	Glycoside	NA (UISO), NA (HCT-15), NA (OVCAR)	
				Stansin 3	Glycoside	NA (UISO), NA (HCT-15), NA (OVCAR)	
				Stansin 4	Glycoside	NA (UISO), NA (HCT-15), NA (OVCAR)	
				Stansin 5	Glycoside	4 (UISO), NA (HCT-15), 1.5 (OVCAR)	
Euphorbiaceae	*Jatropha neopauciflora* Pax	Bk	Chl:MeOH	Calenduladiol	Terpene	NA (U-251), NA (K562)	García and Delgado (2006)
				(3β,16β)-16-hydroxylup-20(29)-en-3-yl (*E*)-3-(4-hydroxyphenyl)prop-2-enoate	Terpene	NA (U-251), NA (K562)	
Fabaceae	*Calliandra californica* Benth.	Rt	Hex, EtOAc, EtOH	Escobarine A	Terpene	1.64 (U-251), 1.7 (PC-3), 0.83 (K-562), 1.33 (HCT-15), 0.2 (MCF-7)	Encarnación-Dimayuga et al. (2006)
				Escobarine B	Terpene	3.48 (U-251), 1.80 (PC-3), 1.98 (K-562), 2.02 (HCT-15), 2.34 (MCF-7)	
	Eysenhardtia polystachya (Ortega) Sarg.	Bk and trunks	Chl:MeOH	(3*S*)-7-Hydroxy-2′,3′,4′,5′,8-pentamethoxyisoflavan	Flavonoid	3.8 (KB), NA (P-388), NA (UISO)	Alvarez et al. (1998)
				(3*S*)-3′,7-Dihydroxy-2′,4′,5′,8-tetramethoxyisoflavan	Flavonoid	3.0 (KB), NA (P-388), NA (UISO)	
				(3*S*)-2′,3′,4′,5′,8-Pentamethoxy-7-*O*-acetylisoflavan	Flavonoid	NA (KB), NA (P-388), NA (UISO)	
				(3*S*)-2′,4′,5′,8-Tetramethoxy-3′,7-*O*-diacetylisoflavan	Flavonoid	NA (KB), NA (P-388), NA (UISO)	
				Isoduartin	Flavonoid	2.63 (KB), NA (P-388), NA (UISO)	

Gelsemiaceae	*Gelsemium sempervirens* (L.) J. St.-Hil.	Sm	MeOH	12β-hydroxy-pregna-4,16-diene-3,20-dione	Pregnane	2.0 (KB), 0.7 (P-388)	Schun and Cordell (1987)
Geraniaceae	*Geranium niveum* S. Watson	Rt	MeOH:Chl	Geranin A	Flavonoid	NA (MCF-7), NA (HT-29), NA (A-549)	Calzada et al. (1999)
				Geranin B	Flavonoid	NA (MCF-7), NA (HT-29), NA (A-549)	
Lamiaceae	*Hyptis pectinata* (L.) Poit	Ap	Chl	Pectinolide A	pyrone	1.0 (BC-1), 1.7 (HT), 0.9 (Lu-1), 0.7 (Mel-2), 1.0 (Col-2), 1.8 (KB), 1.8 (KB-V1), 0.9 (P388), 1.4 (A431), 0.7 (LNCaP), 3.6 (ZR75-1)	Pereda-Miranda et al. (1993), Fragoso-Serrano et al. (2005)
				Pectinolide B	Pyrone	2.5 (BC-1), 2.3 (HT), 3.8 (Lu-1), 2.2 (Mel-2), 1.1 (Col-2), 1.4 (KB), 2.0 (KB-V1*), 0.1 (P388), 0.6 (A431), 0.9 (LNCaP), 1.6 (ZR75-1)	
				Pectinolide C	Pyrone	2.0 (BC-1), 1.8 (HT), 2.3 (Lu-1), 3.3 (Mel-2),1.6 (Col-2), 1.7 (KB), 3.2 (KB-V1*), 2.2 (P388), 0.8 (A431), 0.8 (LNCaP), 1.9 (ZR75-1)	
				Hyptolide	Lactone	2.4 (BC-1), NA (HT), NA (Lu-1), NA (Mel-2), NA (Col-2), 3.6 (KB), NA (KB-V1*), 1.6 (P388), 3.7 (A431), NA (LNCaP), NA (ZR75-1)	
				Boronolide	Lactone	2.8 (BC-1), NA (HT), 3.9 (Lu-1), 3.3 (Mel-2), 4.0 (Col-2), 4.0 (KB), NA (KB-V1*), 1.0 (P388), NA (A431), 3.2 (LNCaP), NA (ZR75-1)	
				Deacetylepiolguine	Lactone	NA (BC-1), NA (HT), 3.3 (Lu-1), NA (Mel-2), 3.0 (Col-2), 2.9 (KB), 3.4 (KB-V1*), 0.4 (P388), 1.9 (A431), 1.8 (LNCaP), NA (ZR75-1)	
				Pectionolide H	Pyrone	NA (KB)	
	Hyptis spicigera Lam.	Ap	Chl:MeOH	19-Acetoxy-2R,7R,15-trihydroxylabda-8(17),(13*Z*)-diene	Terpene	NA (HCT-15), NA (KB)	Fragoso-Serrano et al. (1999)
				15,19-diacetoxy-2R,7Rdihydroxylabda-8(17),(13*Z*)-diene	Terpene	NA (HCT-15), NA (KB)	
				7R,15,19-triacetoxy-2R-hydroxylabda-8(17),(13*Z*)-diene	Terpene	NA (HCT-15), NA (KB)	
				19-Acetoxy-2R,7R-dihydroxylabda-8(17),(13*Z*)-dien-15-al	Terpene	NA (HCT-15), NA (KB)	
				19-Acetoxy-7R,15-dihydroxylabda-8(17),(13*Z*)-dien-2-one	Terpene	NA (HCT-15), NA (KB)	
				19-acetoxy-2R,7R-dihydroxylabda-14,15-dinorlabd-8(17)-en-13-one	Terpene	NA (HCT-15), NA (KB)	
				2R,7R,15,19-tetrahydroxy-*ent*-labda-8(17),(13*Z*)-diene	Terpene	NA (HCT-15), NA (KB)	
	Hyptis verticillata Jacq.	Ap	Hex:Chl	*5*-Methoxydehydropodophyllotoxin	Lignan	NA (P-388), NA (A431), NA (BC-1), NA (Col-2), NA (HT), NA (KB), NA (KB-V1*), NA (LNCaP), NA (Lu-1), NA (U-373), NA (ZR-75-1)	Novelo et al. (1993)

Table 4 (*Continued*)

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
				Dehydro-β-peltatinmethyl ether	Lignan	1.8 (P-388), NA (A431), 2.9 (BC-1), 3.2 (Col-2), 3.4 (HT), 2.2 (KB), NA (KB-V1*), 3.2 (LNCaP), NA (Lu-1), NA (U-373), NA (ZR-75-1)	
				Dehydropodophyllotoxin	Lignan	NA (P-388), NA (A431), NA (BC-1), NA (Col-2), NA (HT), NA (KB), NA (KB-V1*), NA (LNCaP), NA (Lu-1), NA (U-373), NA (ZR-75-1)	
				Deoxydehydropodophyllotoxin	Lignan	NA (P-388), NA (A431), NA (BC-1), NA (Col-2), NA (HT), NA (KB), NA (KB-V1*), NA (LNCaP), NA (Lu-1), NA (U-373), NA (ZR-75-1)	
				(−)-Yarein	Lignan	0.4 (P-388), NA (A431), 0.05 (BC-1), 0.08 (Col-2), 0.07 (HT), 0.08 (KB), 0.06 (KB-V1*), 0.16 (LNCaP), 0.1 (Lu-1), 0.3 (U-373), 0.5 (ZR-75-1)	
				4′-Demethyldeoxypodophyllotoxin	Lignan	0.005 (P-388), 0.08 (A431), 0.01 (BC-1), 0.03 (Col-2), 0.01 (HT), 0.01 (KB), 0.02 (KB-V1*), 0.02 (LNCaP), 0.03 (Lu-1), 0.1 (U-373), 2.1 (ZR-75-1)	
				Isodeoxypodophyllotoxin	Lignan	NA (P-388), NA (A431), NA (BC-1), NA (Col-2), NA (HT), NA (KB), NA (KB-V1*), NA (LNCaP), NA (Lu-1), 2.9 (U-373), NA (ZR-75-1)	
				Deoxypicropodophyllin	Lignan	0.1 (P-388), NA (A431), 2.1 (BC-1), 0.3 (Col-2), 0.2 (HT), 0.1 (KB), 0.7 (KB-V1*), 0.2 (LNCaP), 0.09 (Lu-1), 0.1 (U-373), 0.6 (ZR-75-1)	
				β-Apopicropodophyllin	Lignan	>0.002 (P-388), NA (A431), 0.001 (BC-1), 0.01 (Col-2), 0.003 (HT), 0.05 (KB), 0.06 (KB-V1*), 0.01 (LNCaP), 0.002 (Lu-1), 0.001 (U-373), 2.0 (ZR-75-1)	
	Salvia pachyphylla Epling ex Munz	Ap	Aco	Pachyphyllone	Terpene	NA (A-2780), NA (SW-1573), NA (WiDr), NA (T-47D), NA (HBL-100)	Guerrero et al. (2006)
				Carnosol	Terpene	1.18 (A-2780), 3.3 (SW-1573), NA (WiDr), NA (T-47D), 1.28 (HBL-100)	
				20-Deoxocarnosol	Terpene	1.7 (A-2780), NA (SW-1573), NA (WiDr), NA (T-47D), 1.45 (HBL-100)	
				Isorosmanol	Terpene	NA (A-2780), NA (SW-1573), NA (WiDr), NA (T-47D), NA (HBL-100)	
				5,6-Didehydro-*O*-methylsugiol	Terpene	NA (A-2780), NA (SW-1573), NA (WiDr), NA (T-47D), NA (HBL-100)	
				Rosmadial	Terpene	NA (A-2780), NA (SW-1573), NA (WiDr), NA (T-47D), NA (HBL-100)	
				16-Hydroxycarnosol	Terpene	1.25 (A-2780), 3.09 (SW-1573), NA (WiDr), NA (T-47D), 1.23 (HBL-100)	
Meliaceae	*Swietenia humilis* Zucc.	Sd	Hex	Humilinolide A	Limonoid	NA (A-549), NA (MCF-7), NA (HT-29)	Jimenez et al. (1997)
				Humilinolide B	Limonoid	NA (A-549), NA (MCF-7), NA (HT-29)	
				Humilinolide C	Limonoid	NA (A-549), NA (MCF-7), NA (HT-29)	
				Humilinolide D	Limonoid	NA (A-549), NA (MCF-7), NA (HT-29)	
Picramniaceae	*Picramnia antidesma* subsp. *fessonia* (DC.) W. W. Thomas	Rb	Et_2O MeOH	10-Epi-uveoside	Glycoside	0.3 (KB), 1.13 (HCT), NA (OVCAR), 2.22 (SQC-1)	Hernández-Medel and Pereda-Miranda (2002)
				Uveoside	Glycoside	2.21 (KB), 2.31 (HCT), 2.26 (OVCAR), NA (SQC-1)	

				Picramnioside E	Glycoside	1.79 (KB), 3.27 (HCT), NA (OVCAR), 1.47 (SQC-1)	
				Picramnioside D	Glycoside	1.69 (KB), 3.32 (HCT), 2.9 (OVCAR), 2.16 (SQC-1)	
				Saroside	Glycoside	NA (KB), NA (HCT), NA (OVCAR), NA (SQC-1)	
				Mayoside	Glycoside	NA (KB), NA (HCT), NA (OVCAR), NA (SQC-1)	
Piperaceae	*Piper aduncum* L.	Lv	Chl	2′, 6′-Dihydroxy-4′-methoxydihydrochalcone	Chalcone	NA (KB)	Orjala et al. (1994)
				2′, 6′, 4-Trihydroxy 4′methoxydihydrorhalcone	Chalcone	NA (KB)	
				Piperaduncin A	Chalcone	2.3 (KB)	
				Piperaduncin B	Chalcone	NA (KB)	
				Piperaduncin C	Chalcone	NA (KB)	
Poaceae	*Zea mays* L	Ftgerm	MeOH H_2O	13-Hydroxy-10-oxo-9-methoxy-*trans*-11-octadecenoic-acid	Fatty acid	NA (MCF-7), NA (MDA-MB157), NA (MDA-MB415), NA (MDA-MB468), NA (SK-BR-3), NA (HCT-116), NA (SK-CO-1), NA (SW-480), NA (SW-620), NA (T-84), NA (WiDR), NA (AGS), NA (HS746T), NA (P-388)	Kuga et al. (1993), Hayashi et al. (1996)
				13-Hydroxy-10-oxo-*trans*-11-octadecenoic-acid	Fatty acid	NA (MCF-7), NA (MDA-MB157), NA (MDA-MB415), 3.3 (MDA-MB468), 3.1 (SK-BR-3), 1.6 (HCT-116), NA (SK-CO-1), 3.9 (SW-480), 4.0 (SW-620), NA (T-84), NA (WiDR), 3.9 (AGS), NA (HS746T), 2.6 (P-388)	
				11(*E*)-10-oxo-11-octadecen-13-olide-acid	Fatty acid	0.9 (P388), 2.8 (Ehrlich), 1.7 (B16), 2.2 (KB), 1.9 (S180)	
Rubiaceae	*Hintonia latiflora* Sessé & Moc. ex DC. Bullock	Sb	MeOH	7-Methylluteolin	Flavonoid	NA (KB)	Del Rayo Camacho et al. (2004)
				5-*O*-β-D-galactopyranosyl)-3′,4′-dihydroxy-7-methoxy-4-phenylcoumarin	Coumarin	NA (KB)	
				5-*O*-β-D-(glucopyranosyl)-3′,4′-dlhydroxy-7-methoxy-4-phenylcoumarin	Coumarin	NA (KB)	
				4′,5′-dihydroxy-7-methoxy-4-phenyl 5, 2′oxidocoumarin	Coumarin	NA (KB)	
Sapotaceae	*Manilkara zapota* (L.) Van Royen	Ft	MeOH	Methyl 4-*O*-galloylchlorogenate	Polyphenol	NA (HCT-116), NA (SW-480)	Ma et al. (2003)
				4-*O*-Galloylchlorogenic acid	Polyphenol	NA (HCT-116), NA (SW-480)	
Valerianaceae	*Valeriana sorbifolia* Kunth	Ap	Hex: MeEtAco:MeOH	Sorbifolivaltrate A	Valepotriate	1.19 (PC-3M)	Xu et al. (2007)
				Sorbifolivaltrate B	Valepotriate	NA (PC-3M)	

Table 4 (*Continued*)

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
				Sorbifolivaltrate C	Valepotriate	NA (PC-3M)	
				Sorbifolivaltrate D	Valepotriate	NA (PC-3M)	
				Isovaltrate	Valepotriate	1.3 (PC-3M)	
Viscaceae	*Phoradendron reichenbachianum* (Seem.) Oliver	Ap	Aco	Moronic acid	Terpene	3.6 (HCT-15), 3.9 (UISO), 5.3 (KB)	Rios et al. (2001a)
				3,4 Seco-olean-18-ene-3, 20 dioic acid	Terpene	NA (HCT-15), NA (UISO), NA (KB)	
	Phoradendron serotinum (Raf.) M. C. Johnst.	Lv	Aco	Phoratoxin B	Thionin	1.71 (RPMI 8226-S), 1.47 (RPMI 8226-LR5), 1.81 (RPMI 8226-dox40), 1.02 (U-937 GTB), 0.88 (U-937 Vcr), 0.18 (NCI-H69), 1.12 (NCI-H69 AR), 1.61 (CCRF-CEM), 1.56 (CEM-VM-1), 2.88 (ACHN)	Johansson et al. (2003)
				Phoratoxin C	Thionin	0.87 (RPMI 8226-S), 0.87 (RPMI 8226-LR5), 0.63 (RPMI 8226-dox40), 0.43 (U-937 GTB), 0.48 (U-937 Vcr), 0.19 (NCI-H69), 1.12 (NCI-H69 AR), 0.97 (CCRF-CEM), 0.73 (CEM-VM-1), 1.65 (ACHN)	
				Phoratoxin D	Thionin	1.16 (RPMI 8226-S), 1.16 (RPMI 8226-LR5), 0.99 (RPMI 8226-dox40), 0.64 (U-937 GTB), 0.6 (U-937 Vcr), 0.19 (NCI-H69), 1.03 (NCI-H69 AR), 1.63 (CCRF-CEM), 0.95 (CEM-VM-1), 2.75 (ACHN)	
				Phoratoxin E	Thionin	2.09 (RPMI 8226-S), 1.85 (RPMI 8226-LR5), 2.09 (RPMI 8226-dox40), 1.7 (U-937 GTB), 1.41 (U-937 Vcr), 0.18 (NCI-H69), 1.26 (NCI-H69 AR), 2.19 (CCRF-CEM), 1.66 (CEM-VM-1), 2.82 (ACHN)	
				Phoratoxin F	Thionin	2.19 (RPMI 8226-S), 1.75 (RPMI 8226-LR5), 2.48 (RPMI 8226-dox40), 1.51 (U-937 GTB), 1.12 (U-937 Vcr), 0.18 (NCI-H69), 1.46 (NCI-H69 AR), 2.43 (CCRF-CEM), 2.04 (CEM-VM-1), NA (ACHN)	

Nature of the extracts: BuOH, buthanol; Chl, chloroform; DCM, dichloromethane; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexane; H_2O, aqueous; MeOH, methanol; MeEtAco, methy ethyl acetone; PE, petroleum ether; Aco, acetone, Et_2O, dy ethyl ether.
Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Wp, whole plant.
Cell lines: 1301, lymphoblastic leukemia; A-2780, ovarian carcinoma; A-431, epidermoid carcinoma; A-498, human kidney carcinoma; A-549, human lung carcinoma; ACHN, renal carcinoma drug resistant; AGS, stomach adenocarcinoma; ASK, Atlantic salmon kidney, B16, mouse melanoma; Caco-2, human epithelial colorectal adenocarcinoma; CCRF-CEM, leukemia drug resistant; CEM-VM-1, leukemia durg resistant; COLON, colon carcinoma, DU-145, prostate carcinoma, Ehrlich, ascites tumor; H-460, human large cell lung carcinoma; HBL-100, breast carcinoma; HCT-15 COLADCAR, adherent colon carcinoma; HCT-116, human colorectal carcinoma; HeLa, cervix adenocarcinoma; Hep-2, laryngeal carcinoma, HepG2, hepatocarcinoma; HF-6, human colon carcinoma; HS746T, stomach carcinoma; HT-29, human colon adenocarcinoma; HT1080, human fibrosarcoma; K-562, chronic myeloblastic leukemia, KB, human nasopharynx carcinoma; L5178Y-R, murine lymphoma; LLC-MK2, Rhesus monkey kidney cells; MDA-MB157, breast carcinoma; MDA-MB415, breast carcinoma; MDA-MB468, breast carcinoma; MDCK, canine kidney cells, MCF-7, human breast carcinoma; NCI-H69, small cell lung cancer drug resistant; NCI-H69 AR, small cell lung cancer drug resistant; P-388, mouse leukemia; PACA-2, human pancreatic carcinoma; PC-3, human prostate adenocarcinoma; RPMI 8226-S, mieloma drug resistant; RPMI 8226-LR5, myeloma drug resistant; RPMI 8226-dox40, myeloma drug resistant; S180, murine sarcoma; SK-BR-3 breast carcinoma; SF268, glioma; SiHa, cervix squamous carcinoma; SW480, colon carcinoma; SW620, colon carcinoma; SW-1573, lung carcinoma; T-47D, breast carcinoma; T84, colon adenocarcinoma; TE671, meduloblastoma; U-937, GTB mistiocytic lymphoma drug resistant; U-937 Vcr, mistiocytic lymphoma drug resistant; U-251,human glioma; UACC-62, human melanoma; UISO-SQC-1, squamous cervix carcinoma; OVCAR, ovary carcinoma; WiDR, colon carcinoma.
VI* denotes drug resistance.

Table 5
Cytotoxicity of novel compounds isolated from Mexican plants.

Family	Scientific name	Plant part	Extract	Compound	Group	ED_{50} μg/ml (cell line)	Reference
Annonaceae	*Annona muricata* L.	Lv	EtOH	Annopentocin A	Acetogenin	0.17 (A-549), NA (MCF-7), 1.63 (HT-29), 0.6 (A-498), 1.14 (PC-3), 0.03 (PACA-2)	Zeng et al. (1996)
				Annopentocin B	Acetogenin	0.02 (A-549), 3.56 (MCF-7), 1.64 (HT-29), 0.38 (A-498), 0.21 (PC-3), 0.16 (PACA-2)	
				Annopentocin C, *cis*- and *trans*	Acetogenin	0.02 (A-549), 2.97 (MCF-7), 1.24 (HT-29), 0.26 (A-498), 0.22 (PC-3), 0.43 (PACA-2)	
				Annomuricin-D	Acetogenin	<0.01 (A-549), 0.6 (MCF-7), <0.01 (HT-29), 0.1 (A-498), 1.32 (PC-3), <0.01 (PACA-2)	
	Annona purpurea Moc. & Sessé ex Dunal	Sd	Chl:MeOH	Purpurediolin	Acetogenin	0.443 (A-549), 0.916 (MCF-7), $<10^{-7}$ (HT-29), 1.36 (A-498), 0.353 (PC-3), 1.44 (PACA-2)	Chávez and Mata (1998)
				Purpurenin	Acetogenin	1.29 (A-549), 1.67 (MCF-7), 0.316 (HT-29), 1.25 (A-498), 1.07 (PC-3), 1.98 (PACA-2)	
Asteraceae	*Montanoa leucantha* (Lag.) S. F. Blake	Lv	EtOAc	Leucanthanolide	Terpene	0.57 (KB), 0.93 (P-388)	Oshima et al. (1986)
	Viguiera hypargyrea Greenm.	Ap	DCM:MeOH	8β-(epoxyangeloyloxy)-14-hydroxy-tithifolin	Terpene	1.2 (KB), 1.4 (P-388), 3.6 (KB-VI*)	Villarreal et al. (1994)
				8β-(epoxyangeloyll)-14acetoxy-eupatolide	Terpene	1.5 (KB), 2.8 (P-388), NA (KB-VI*)	
	Viguiera quinqueradiata|(Cav.) A. Gray	Lv	Chl	15-Hydroxyacetyl-leptocarpin	Terpene	1.0 (KB), 1.0 (P-388), NA (KB-VI*)	Villarreal et al. (1994)
Gelsemiaceae	*Gelsemium sempervirens* (L.) J. St.-Hil	Sm	MeOH	12β-hydroxy-5α-pregn-16-ene-3,20 dione	Pregnane	2.8 (KB), 0.9 (P-388)	Schun and Cordell (1987)
Lamiaceae	*Salvia leucantha* Cav.	Ap	Aco	Salvileucalin B	Terpene	NA (A-549), 1.88 (HT-29)	Aoyagi et al. (2008)
Lauraceae	*Persea americana* Mill.	Ft	EtOH	1,2,4Trihydroxynonadecane	Fatty acid	3.0 (A-549), 3.2 (MCF-7), 3.0 (HT-29), 2.7 (A-498), 1.2 (PC-3), NA (PaCa-2)	Oberlies et al. (1998)
				1,2,4-Trihydroxyheptadec-16-ene	Fatty acid	3.4(A-549), NA (MCF-7), 2.6(HT-29), 3.6 (A-498), 0.46 (PC-3), NA (PaCa-2)	
				1,2,4-Trihydroxyheptadec-16-yne	Fatty acid	NA (A-549), NA (MCF-7), NA (HT-29), NA (A-498), 0.06 (PC-3), NA (PaCa-2)	
Poaceae	*Zea mays* L.	Ft	MeOH	13-hydroxy-10-oxo-*trans*-11-octadecenoic-acid	Fatty acid	NA (MCF-7), NA (MDA-MB157), NA (MDA-MB415), 3.3 (MDA-MB468), 3.1 (SK-BR-3), 1.6 (HCT-116), NA (SK-CO-1), 3.9 (SW-480), 4.0 (SW-620), NA (T-84), NA (WiDR), 3.9 (AGS), NA (HS746T), 2.6 (P-388)	Kuga et al. (1993), Hayashi et al. (1996)
		Germ	H_2O	11(*E*)-10-oxo-11-octadecen-13-olide-acid	Fatty Acid	0.9 (P388), 2.8 (Ehrlich), 1.7 (B16), 2.2 (KB), 1.9 (S180)	

Nature of the extracts: BuOH, buthanol; Chl, chloroform; DCM, dichloromethane; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexane; H_2O, aqueous; MeOH, methanol; MeEtAco, methy ethyl acetone; PE, petroleum ether; Aco, acetone; Et_2O, dy ethyl ether.
Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Wp, whole plant.
Cell lines: A-498, human kidney carcinoma; A-549, human lung carcinoma; AGS, stomach adenocarcinoma; B16, mouse melanoma; Ehrlich, ascites tumor; HCT-116, human colorectal carcinoma; HS746T, stomach carcinoma; HT-29, human colon adenocarcinoma; KB, human nasopharynx carcinoma; MCF-7, human breast carcinoma; MDA-MB157, breast carcinoma; MDA-MB415, breast carcinoma; MDA-MB468, breast carcinoma; P-388, mouse leukemia; PACA-2, human pancreatic carcinoma; PC-3, human prostate adenocarcinoma; S180, murine sarcoma; SK-BR-3, breast carcinoma; SK-CO-1, colon adenocarcinoma; SW480, colon carcinoma; SW620, colon carcinoma; T84, colon adenocarcinoma; WiDR, colon carcinoma.
VI* denotes drug resistance.

Table 6
Anti-tumor effects of compounds isolated from Mexican plants.

Family	Scientific name	Plant part	Extract	Compound	Animal system	Dose (mg/kg)	Route of administration	Time (days)	Tumor system (tumor inhibition %)	Reference
Annonaceae	*Annona diversifolia* Saff. Sd	Sd	Hex	Laherradurin	Athymic mice	1.5	Sc	20	HeLa (54), SW-480 (44)	Schlie-Guzmán et al. (2009)
						7.5	Sc		HeLa (64), SW-480 (60)	
				Cherimolin-2	Athymic mice	1.5	Sc		HeLa (30)	
						7.5	Sc		HeLa (43)	
Asteraceae	*Hymenoxys odorata* DC.	Ap	Aco	Hymenovin	C3H mice	10	Sc	21	C3H mouse mammary carcionoma (60)	Ivie et al. (1975)
Lamiaceae	*Hyptis emory* Torr.	Ap	Chl	Betulinic acid	Sprague rats	300	Im	15	Walker carcinoma 5WA16 (48)	Sheth et al. (1972)
						500	Im		Walker carcinoma 5WA16 (85)	
Scrophulariaceae	*Capraria biflora* L.	Rt	PE	Biflorin	Swiss mice	25	Ip	8	Sarcoma 180 (15)	Vasconcellos et al. (2005)
						50	Ip		Sarcamo 180 (50)	
						25	Ip		Ehrlich (12)	
						50	Ip		Ehrlich (45)	

Nature of the extracts: BuOH, buthanol; Chl, chloroform; DCM, dichloromethane; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexane; H_2O, aqueous; MeOH, methanol; MeEtAco, methy ethyl acetone; PE, petroleum ether; Aco, acetone; Et_2O, dy ethyl ether.
Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Wp, whole plant.
Route of administration: Im, intramuscular; Ip, intraperitoneal; It, intratumoral; Iv, intravenous; Sc, subcutaneous.

them 77 compounds (41%) have demonstrated active cytotoxicity (Tables 4 and 5). The main types of plant secondary metabolites with the highest number of compounds are: glycosides (50), terpenes (49), lignans (15), acetogenins (13) and flavonoids (11). However, only 15 terpenes (31% of total terpenes) and 9 glycosides (18% of total glycosides) show active cytotoxic properties. In contrast, 13 acetogenins (87% of total acetogenins) and 12 lignans (80% of total lignans) exert active cytotoxic effects. Up to now, 17 compounds, all of them active, have been reported to be present only in Mexican plant species (Table 5). Of these compounds, the main types of secondary metabolites are acetogenins (6), terpenes (5) fatty acids (5) and pregnanes (1). The isolation and characterization of the active compounds warrant more attention. Annonaceous acetogenins constitute a group of secondary metabolites that might be found to be exclusively isolatable from species of the Annonaceae family. Acetogenins are the most active cytotoxic compounds found in Mexican plant species and the *Annona* species are an important source of these compounds. In fact, 66% of total acetogenins are found exclusively in Mexican plants. However, only laherradurin and cherimolin-2, isolated from *Annona diversifolia* have been tested *in vivo* (Schlie-Guzmán et al., 2009), and the results indicated that laherradurin 7.5 mg/kg inhibited tumor growth in nu/nu mice, induced by HeLa (64%) and SW480 (60%) cells, whereas cherimolin-2 tested at 7.5 mg/kg inhibited tumor growth induced by HeLa (43%) cells.

Although the isolation and purification of compounds from active plant extracts have been extensive, many compounds with promising cytotoxic activities (even active in cancer cell lines resistant to anticancer drugs), remain to be tested on *in vivo* systems. Only 5 compounds have been evaluated in animal models for their anti-neoplastic effects (Table 6). Although there is no index value to consider that a compound is active on *in vivo* systems; currently anti-cancer drugs inhibit 50% of growth tumor at concentrations less than 15 mg/kg body weight. Taking this value into account, laherradurin and cherimolin-2 from *Annona diversifolia*, and hymenovin from *Hymenoxys odorata*, might be considered as active *in vivo* (Table 6). However, many anti-cancer drugs at these concentrations induce high toxic effects such as body weight loss in experimental animals. Therefore, it might be highly desirable to continue looking for new anti-tumor compounds that induce low toxic effects.

7. Mechanisms of action of Mexican plant extracts and their active compounds

A handful of Mexican plant extracts and their active compounds have been studied for their mechanisms of action. An aqueous extract of *Justicia spicigera* leaves induced apoptosis in the human leukemia TF-1, human cervical cancer CaLo and InBl cell lines as determined by TUNEL reaction (Cáceres-Cortés et al., 2001). A methanol extract of *Phaseolus vulgaris* seeds decreased the number of human cervical cancer HeLa cells in the G_0/G_1 phase by 17% and increased apoptosis by 18%, when compared to untreated cells (Aparicio-Fernández et al., 2006). A hexanic extract of *Gymnosperma glutinosum* leaves produced apoptosis in murine lymphoblastic L5178Y cells as determined by DNA fragmentation (Gomez-Flores et al., 2009). It is important to study the mechanism of action of active plant extracts and their compounds in order to propose combinatorial employment of extracts or compounds with different mechanisms of action, to improve anti-cancer therapies.

8. Mexican plants used for empirical treatment of diseases with cancer symptomatology without scientific studies

On the other hand, the families that contain the highest number of plants used empirically to treat cancer-like diseases that

Table 7
Mexican plants used for empirical treatment of diseases with cancer symptomatology without scientific studies.

Family	Scientific name	Common name	Plant part	Popular use	Reference
Acanthaceae	*Ruellia malacosperma* Greenm.	Hierba del chivo	Lv	DER	Mendieta and Del Amo (1981)
Agavaceae	*Agave atrovirens* Karw. Ex Salm-Dyck.	Maguey	Lv	VEN, INF	Martínez (1989)
	Agave ixtli Karw.	Caña de jabali	Rt	UR, VEN	Mendieta and Del Amo (1981)
Anacardiaceae	*Metopium brownei* (Jacq.) Urb.	chechén negro	Bk	DER	Flores and Ricalde (1996)
Apiaceae	*Eryngium carlinae* F. Delaroche	Hierba del sapo	Wp	DER	Escobar-Linares (1999)
Apocynaceae	*Echites yucatanensis* Millsp. ex Standl.	Liana	Lv	DER	Flores and Ricalde (1996)
	Plumeria alba L.	Flor de mayo	Latex	INF	Mendieta and Del Amo (1981)
	Stemmadenia mollis Benth.	Chiguilillo	Lv	RES	Argueta et al. (1994)
	Stemmadenia pubescens Benth.	Cojon de gato	Lv	INF	Argueta et al. (1994)
	Thevetia gaumeri Hem.	Akits de playa	Ap	INF, DER	Mendieta and Del Amo (1981)
Aristolochiaceae	*Aristolochia pilosa* Kunth	Guaco	Rt	INF	Martínez (1989)
Asclepiadaceae	*Asclepias glaucescens* Kunth	Oerja de liebre	Lv	INF	Hernández (1959)
	Asclepias similis Hemsl.	Panyattez	Latex	DER	Fernandez-Brewer et al. (2008)
Asteraceae	*Archibaccharis serratifolia* (Kunth) S.F. Blake	Guacor	Lv	INF	Martínez (1989)
	Artemisia ludoviciana subsp. *mexicana* (Willd. ex Spreng.) D.D. Keck	Estafiate	Ap	INF	Baytelman-Goldenberg (1980)
	Aster gymnocephalus (DC.) A. Gray	Árnica morada	Wp	INF	González (1984)
	Barkleyanthus salicifolius (Kunth) H. Rob. & Brettell	Jarilla	Ap	INF	Escobar-Linares (1999)
	Calea ternifolia Kunth	Prodigiosa	Br	GI	Escobar-Linares (1999)
	Cirsium mexicanum DC.	Naranja	Ap	UR	Andrade-Cetto (2009)
	Pseudognaphalium oxyphyllum DC.	Gordolobo	Wp	INF	López and Hinojosa (1988)
	Pseudognaphalium viscosum (Kunth) Anderb.	Gordolobo	Br	GI	López and Hinojosa (1988)
	Montanoa tomentosa Cerv.	Zaopatle	Lv	WOM	Martínez (1989)
	Packera candidissima (Greene) W.A. Weber & Á Löve	Té milagro	Wp	GI	González-Elizondo et al. (2004)
	Verbesina crocata (Cav.) Less.	Capitaneja anaranjada	Fw	DER	Martínez (1989)
Basellaceae	*Anredera vesicaria* (Lam.) C.F. Gaertn.	Kaaïxicheĭel	Rt	INF	Ankli et al. (1999)
Bignoniaceae	*Crescentia cujete* L.	Jicara	Fr	INF	Argueta et al. (1994)
	Tabebuia rosea (Bertol.) DC.	Roble	Bk	INF	Graham et al. (2000)
Boraginaceae	*Cordia alliodora* (Ruiz & Pav.) Oken	Aguardientillo	Fw	RES	Niembro (1986)
	Ehretia tinifolia L.	Tlalhuacate	Lv	INF	Hernández (1959)
	Tournefortia densiflora M. Martens & Galeotti	Tlachichinol	Ap	GI	Escobar-Linares (1999)
Brassicaceae	*Lepidium virginicum* L.	Lentejilla	Wp	GI	González (1984)
Bromeliaceae	*Ananas comosus* (L.) Merr.	Piña	Ft	INF	Escobar-Linares (1999)
Buddlejaceae	*Buddleia cordata* Kunth	Tepozan	Lv	UR	Martínez (1989)
Cactaceae	*Ferocactus latispinus* (Haworth) Britton et Rose	Biznaga	Ft	INF	Escobar-Linares (1999)
	Isolatocerues dumortieri (Scheidw.) Backeb.	Organo	Sm	DER	Escobar-Linares (1999)
	Lophocereus schottii (Egelm.) D.R. Hunt	Garambullo	St	UR	Encarnacion and Contreras (1992)
Caryophyllaceae	*Drymaria gracilis* Schltdl. & Cham.	Candelilla	Ap	DER	Graham et al. (2000)
Celastraceae	*Elaeodendron trichotomum* (Turcz.) Lundell	Mangle	Wp	INF	Graham et al. (2000)
Chenopodiaceae	*Dysphania ambrosioides* (L.) Mosyakin & Clemants	Epazote	Ap	RES	Baytelman-Goldenberg (1980)
Chrysobalanaceae	*Licania arborea* Seem.	Cacahuananche	Bk	DER	Cabrera (1958)
Commelinaceae	*Commelina tuberosa* L.	Hierba de pollo	Ap	INF	Escobar-Linares (1999)
Convolvulaceae	*Ipomoea bracteata* Cav.	Empanaditas	Ap	INF	Escobar-Linares (1999)
	Turbina corymbosa (L.) Raf.	Manea de toro	Ap	INF	Hernández (1959)
Costaceae	*Costus mexicanus* Liebm.	Diente de jabalí	Ap	DER	González (1984)
	Costus spicatus (Jacq.) Sw.	Caña de jabali	Sm	UR	Martínez (1989)
Crassulaceae	*Sedum dendroideum* Moc. & Sessé ex DC.	Siempreviva	Lv	DER	Hernández (1959)
Cucurbitaceae	*Cucurbita foetidissima* Kunth	Calabacilla	Rt	DER	González (1984)
	Sechium edule (Jacq.) Sw.	Chayote	Ap	INF	Escobar-Linares (1999)
Euphorbiaceae	*Acalypha adenostachya* Mull. Arg.	Hierba del cancer	Lv	WOM	López and Hinojosa (1988)
	Acalypha alopecuroides Jacq.	Hierba del cancer	Lv	RES, INF	Hernández (1959)
	Acalypha californica Benth.	Hierba del cáncer	Br	GI	Moreno-Salazar et al. (2008)
	Acalypha phleoides Cav.	Hierba del cáncer	Ap	INF	Gispert and Rodriguez (1998)
	Chamaesyce hirta (L.) Millsp.	Golondrina	Lv	VEN, RES, GI	Mendieta and Del Amo (1981)
	Cnidoscolus aconitifolius (Mill.) I.M. Johnst.	Chaya	Thorns	UR	González (1984)
	Croton alamosanus Rose	Croton	Br	GI	Moreno-Salazar et al. (2008)
	Croton flavens L.	Ikaban	Lv	DER	Flores and Ricalde (1996)

Table 7 (*Continued*)

Family	Scientific name	Common name	Plant part	Popular use	Reference
	Croton glabellus L.	Cascarillo	Lv	GI	González (1984)
	Euphorbia heterophylla L.	Picachali	Sm	DER	Flores and Ricalde (1996)
	Euphorbia lomelii V.W. Steinm.	Esqueleto de la muerte	Sm	DER	Escobar-Linares (1999)
	Euphorbia tanquahuete Sessé & Moc.	Pega hueso	Wp	INF	González (1984)
	Hura polyandra Baill.	Haba de san Ignacio	Lv	DER	Flores and Ricalde (1996)
	Jatropha curcas L.	Coahuixtle	Lv	DER	Escobar-Linares (1999)
	Sapium macrocarpum Müll. Arg.	Chilamate	Sm	DER	Flores and Ricalde (1996)
Fabaceae	*Aeschynomene fascicularis* Schltdl. & Cham.	Pegapega	Lv	INF	Mendieta and Del Amo (1981)
	Acacia farnesiana (L.) Willd.	Hizache	Lv	DER	Cabrera (1958)
	Acacia macracantha Humb. & Bonpl. exWilld.	Algarrobo	Sm	GI	Mendieta and Del Amo (1981)
	Centrosema pubescens Benth.	Centro	Fw	DER	Graham et al. (2000)
	Leucaena esculenta (Moc. & Sessé ex DC.) Benth.	Guaje	Ft	DER	Escobar-Linares (1999)
	Lysiloma acapulcense (Kunth) Benth.	Tepehuaje	Bk	DER, GI	Escobar-Linares (1999)
	Mimosa brandegei B. L. Rob.	Uña de gato	Ap	DER	Escobar-Linares (1999)
	Pithecellobium dulce (Roxb.) Benth.	Guamúchil	Bk	GI	Encarnación-Dimayuga et al. (1987)
	Prosopis juliflora (Sw.) DC.	Mezquite	Br	DER, GI	Gispert and Rodriguez (1998)
Fagaceae	*Quercus grisea* Liebm.	Encino blanco	Bk	INF	González-Elizondo et al. (2004)
	Quercus rugosa Née	Encino	Bk	GI	Castillo-Juárez et al. (2009)
	Quercus resinosa Liebm.	Roble	Lv	UR	González-Elizondo et al. (2004)
Hypericaceae	*Hypericum pratense* Schltdl. & Cham.	Tenchalita	Lv	INF	Martínez (1989)
Krameriaceae	*Krameria cytisoides* Cav.	Crameria	Rt	GI	Graham et al. (2000)
	Krameria erecta Willd. ex Schult.	Cosahui	Ap	GI	Moreno-Salazar et al. (2008)
Lamiaceae	*Lepechinia caulescens* (Ortega) Epling.	Bretanica	Wp	GI	Graham et al. (2000)
	Salvia coccínea L.	Mirto	Rt	INF	Mendieta and Del Amo (1981)
Lauraceae	*Litsea glaucescens* Kunth	Laurel	Lv	DER	López and Hinojosa (1988)
Loasaceae	*Gronovia scandens* L.	Chichicastle	Lv	INF	Escobar-Linares (1999)
Lythraceae	*Cuphea wrightii* A. Gray	Hierba del cancer	Wp	RES	Cabrera (1958)
	Heimia salicifolia Link	Hierba de San Francisco	Br	DER	Baytelman-Goldenberg (1980)
Malpighiaceae	*Byrsonima crassifolia* (L.) Kunth	Nanche	Br	GI	Martínez (1989)
Malvaceae	*Ceiba aesculifolia* subsp. *parvifolia* (Rose) P.E. Gibbs & Semir	Pochote	Bk	UR	Canales-Martinez et al. (2006)
	Sida rhombifolia L.	Escobilla	Lv	INF	Escobar-Linares (1999)
	Sphaeralcea angustifolia (Cav.) G. Don	Hierba del cancer	Br	GI	Sanchez-Gonzalez et al. (2008)
Martyniaceae	*Proboscidea fragrans* (Lindl.) Decne	Uña de gato	Ap	GI, INF	Gispert and Rodriguez (1998)
Oleaceae	*Fraxinus uhdei* (Wenz.) Linglesh.	Fresno	Lv	INF	Escobar-Linares (1999)
Onagraceae	*Lopezia racemosa* Cav.	Perilla	Ap	GI	Linares-Mazari et al. (1988)
	Oenothera rosea L'Herit. ex Aitón	Hierba del golpe	Lv	DER	González (1984)
Orchidaceae	*Catasetum integerrimum* Hook.	Chinela	Wp	DER	Téllez-Valdés et al. (1989)
Papaveraceae	*Argemone ochroleuca* Sweet	Chicalote	Ap	INF	González (1984)
Pinaceae	*Pinus teocote* Schltdl. & Cham.	Ocote	Resin	INF	Escobar-Linares (1999)
Ranunculaceae	*Clematis dioica* L.	Barbas de viejo	Ap	DER	Martínez (1989)
Rubiaceae	*Psychotria papantlensis* (Oerst.) Hemsl.	Hierba verde	Lv	INF	Argueta et al. (1994)
	Randia echinocarpa Moc. & Sessé ex DC.	Granjel	Lv	GI	Martínez (1989)
Salicaceae	*Salix bonplandiana* Kunth	Sauce	Ap	INF, GI	Escobar-Linares (1999))
	Salix taxifolia Kunth	Taray	Ap	INF	Escobar-Linares (1999)
Sapotaceae	*Pouteria sapota* (Jacq.) H. E. Moore & Stearn	Mamey	Lv	DER, INF	Martínez (1989)
Saururaceae	*Anemopsis californica* Hook. & Arn.	Hierba del mango	Wp	WOM, INF, RES	Olivas-Sanchez (1999)
Scrophulariaceae	*Castilleja arvensis* Schltdl. & Cham.	Hierba del cancer	Lv	RES	Mendieta and Del Amo (1981)
	Castilleja tenuiflora Benth.	Cola de borrego	Fw	RES	Graham et al. (2000)
Selaginellaceae	*Selaginella lepidophylla* (Hook. & Grev.)	Doradilla	Wp	INF	Escobar-Linares (1999)
Solanaceae	*Datura inoxia* Mill.	Toloache	Lv	INF	Argueta et al. (1994)
	Datura stramonium L.	Chamico	Lv	INF	Mendieta and Del Amo (1981)
	Lycopersicum esculentum Mill. var. esculentum	Jitomate	Ft	RES, INF	Hernández (1959)
	Physalis philadelphica Lam.	Tomate	Ap	INF	Hernández (1959)
	Solanum hazenii Britton	Berenjena	Wp	INF	Hernández (1959)
	Solanum tuberosum L.	Pustsekua	Ft	INF	Escobar-Linares (1999)

Table 7 (*Continued*)

Family	Scientific name	Common name	Plant part	Popular use	Reference
Taxodiaceae	*Taxodium mucronatum* Ten	Ahuehuete	Lv	VEN, INF	Martínez (1989)
Urticaceae	*Pilea pubescens* Liebm.	Chichicastle	Lv	DER	Argueta et al. (1994)
Verbenaceae	*Lantana camara* L.	Cinco negritos	Ap	UR	Baytelman-Goldenberg (1980)
	Lippia graveolens Kunth	Oregano	Ap	INF	López and Hinojosa (1988)
	Priva mexicana (L.) Pers.	Hierba del cancer	Ap, Rt	INF	Escobar-Linares (1999)
	Verbena carolina L.	Verbena	Lv	GI	Baytelman-Goldenberg (1980)
Viscaceae	*Phoradendron californicum* Nutt.	Toji	Sm	VEN	Argueta et al. (1994)
	Phoradendron quadrangulare (Kunth) Griseb.	Guacalazuchil	Wp	DER	Cabrera (1958)
Vitaceae	*Cissus verticillata* (L.) Nicolson & C. E. Jarvis	Tripa de judas	Ap	GI	Escobar-Linares (1999)

Plant part used: Ap, aerial parts; Bl, bulbs; Br, branches; Bk, bark; Ft, fruits; If, influoresnce; Lv, leaves; Pt, petiole; Rb, root bark; Rh, rhizomes; Rt, roots; Sb, stem bark; Sd, seeds; Sm, stem; Wp, whole plant. *Popular use*: AP, antiparasitic; DER, dermatological conditions; GI, gastrointestinal disorders; INF, inflammatory diseases; NEU, neurological disorders; RES, respiratory illnesses; UR, urological problems including diabetes; VEN, veneral diseases; WOM, gynecological disorders.

lack scientific studies are: Euphrobiaceae (15), Asteraceae (11), Fabaceae (9), and Solanaceae (6) (Table 7). From these species, *Proboscidea fragrans* (uña de gato) is widely employed in Mexican traditional medicine as an anti-cancer agent. However, no pharmacological validations have been performed. Mexican plants used for diseases with cancer symptomatology are used by traditional medicine in categories such as dermatological and inflammatory diseases (Table 7). In some rural locations, medicinal plants are used as teas, decoctions or infusions for the empirical treatment of parasites, and respiratory, urological, gastrointestinal and neurological disorders. On the other hand, medicinal plants used to treat dermatological conditions, as well as inflammatory and venereal diseases, are commonly employed in the form of topical applications or medicinal baths. In urban areas, medicinal plants used for the empirical treatment of cancer, are sold as "food" or "supplement" products, and prepared as teas, decots, syrups and powders; and less often as capsules and pills (Table 7). The insufficient regulation of the medicinal plant products might be harmful for cancer patients for the following reasons: (i) these formulations might contain pathogenic microorganisms, pesticides, heavy metals, (ii) a misidentified plant might be used, (iii) a different plant than the one originally used for the treatment may be substituted for the same treatment.

Compounds isolated from *Croton cajucara*, *Croton regelianus* and *Croton caracasanus*, distributed in South America, showed cytotoxic effects on human cancer cell lines (Grynberg et al., 1999; Suárez et al., 2009; Bezerra et al., 2009). Active isolated compounds from *Croton regelianus* and *Croton cajacura* showed antitumor effects (Grynberg et al., 1999; Bezerra et al., 2009). Related species from *Euphorbia* genus, collected in Europe and Asia and their isolated compounds, have shown cytotoxic effects on human cancer lines (Amirghofran et al., in press; Duarte et al., 2009). *Euphorbia tirucalli*, distributed from tropical Africa to South America, showed anti-tumor activity in BALB/c mice (Valadares et al., 2006). Ingenol-3-angelate (Ing3A), isolated from the European species *Euphorbia peplus*, is currently in clinical trials for the treatment of squamous cell carcinoma (Li et al., 2010). This might suggest that Mexican Euphrobia and Croton, to mention a few of the Mexican species employed for the empirical treatment of cancer (Table 7) might be good candidates for the discovery of new anti-cancer drugs.

9. Further considerations

Mexico possesses a wide variety of plant species that might be important sources of anti-cancer compounds. In order to avoid the extinction of these plants and their active compounds, it is important to protect and promote the rational exploitation of this source of promising chemical compounds. For instance, Taxol is isolated from *Taxus brevifolia* and *Taxus baccata*, to produce 2.5 kg of this compound, 27,000 tons of *Taxus brevifolia* barks are required and approximately 12,000 trees were cut down (Rates, 2001). It is clearly necessary to partially synthesize anti-cancer compounds and other semi-synthetic analogues in order to obtain large quantities of new anti-cancer drugs. Continuing research should include studies on the mechanisms of action of each plant extract and active compounds to better understand their construction of anti-cancer effects. It is possible that the combinations of active compounds might be tested to obtain better results in cancer therapy. Optimal doses for plant extracts must also be calculated.

No clinical trials have been performed with Mexican plant extracts or their active compounds which might be due to the lack of studies on the toxicological effects of these plants on laboratory animals. It is necessary and important to increase the number of experimental studies and to begin to conduct clinical trials with

those Mexican plants and their active principles with *in vitro* and *in vivo* studies.

10. Conclusions

Despite the widespread use of Mexican plants for the treatment of diseases with cancer symptomatology, there are a very limited number of scientific studies and no clinical trials published on this topic. Clearly, it is time to increase the number of scientific studies and to begin to conduct clinical trials with plants from Mexico. In addition, the mechanisms of action by which plant extracts and their active compounds exert their anti-cancer effects need to be studied.

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