Turk J. Pharm. Sci. 9(2), 241-256, 2012

Review

USES OF SOME *EUPHORBIA* SPECIES IN TRADITIONAL MEDICINE IN TURKEY AND THEIR BIOLOGICAL ACTIVITIES

Serkan ÖZBİLGİN, Gülçin SALTAN ÇİTOĞLU*

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy
06100 Tandoğan-Ankara, TURKEY

Abstract

The genus Euphorbia is the largest in spurge family (Euphorbiaceae), comprising more than 2000 species. Some species of the genus Euphorbia have been used as medicinal plants for the treatment of skin diseases, migraine, and intestinal parasites and as wart cures. Due to the rich cultural heritage and relatively rich flora, a wealth of knowledge on traditional and folk medicine has been accumulated in Turkey. Some Euphorbia species have been using to treat skin diseases and wounds in different provinces in Turkey. The used parts of the Euphorbia species include roots, seeds, latex, stem wood, stem barks, leaves, and whole plants. Euphorbias have curative properties due to presence of various chemicals, which are found as secondary metabolites in these plants. Plants in the family Euphorbiaceae are well known for the chemical diversity of their isoprenoid constituents. Diterpenoids are majority of the genus with many different skeletons such as jatrophanes, lathyranes, tiglianes, ingenanes, myrsinanes, etc. In addition, sesquiterpenoids, flavonoids and steroids were also obtained. The compounds isolated from genus Euphorbia and extracts perform many different biological activities, including antiproliferative, cytotoxic, antimicrobial and anti-inflammatory, anticancer and antioxidant activities etc.

Key words: *Euphorbiaceae, Euphorbia, Traditional medicine, Turkey, Biological activity.*

Türkiye'de Geleneksel Tedavide Kullanılan Bazı Euphorbia Türleri ve Biyolojik Aktiviteleri

Euphorbia cinsi, Sütleğengiller (Euphorbiaceae) familyasında 2000'den fazla türle en büyük cinstir. Bazı Euphorbia türleri deri hastalıklarının tedavisinde, yaralarda, migrende ve kurt düşürücü amaçla kullanılmaktadır. Zengin kültürel miras ve zengin floraya sahip Türkiye'de geleneksel tedavi ve halk ilaçları açısından büyük bir birikim vardır. Bazı Euphorbia türleri Türkiye'nin farklı bölgelerinde deri hastalıkları ve yara iyi edici olarak kullanılmaktadır. Euphorbia türlerinin kökleri, tohumları, lateksi, gövdenin odun ve kabukları, yaprakları ve bitkinin tamamı kullanılmaktadır. Euphorbia'ların sekonder metabolitleri olan çeşitli kimyasal maddelere bağlı tedavi edici özellileri vardır. Euphorbiaceae familyasına ait bitkiler isoprenoid yapısında maddeler taşırlar. Jatrofanlar, latiranlar, tigliyanlar, ingenanlar, mirsinanlar gibi iskeletlere sahip diterpenoidler cinsin ana etken madde grubudur. Buna ek olarak seskiterpenoidler, flavonoidler ve steroidleri de içerirler. Euphorbia cinsinden ve ekstrelerinden izole edilen bileşiklerin koruyucu, sitotoksik, antimikrobiyal, antiinflamatuvar, antikanser ve antioksidan vb. etkileri vardır.

Anahtar kelimeler: *Sütleğengiller, Euphorbia, Geleneksel tedavi, Türkiye, Biyolojik aktivite.*

***Correspondence:** E-mail: gulcin.saltan@pharmacy.ankara.edu.tr; Tel: +90 312 203 30 88

INTRODUCTION

Humans have always made use of their native flora, not just as a source of food, but also for fuel, medicines, clothing, home construction, and chemical production. Traditional knowledge of plants and their properties has always been transmitted from generation to generation through the natural course of every day life (1).

Globally, millions of people in the developing world rely on medicinal plants for primary health care, income generation and livelihood improvement. Between 50.000 and 70.000 plant species are known to be used in traditional and modern medicinal systems throughout the world (2).

Plant natural products have been a historically important component in the treatment and prevention of illness. Plants are a rich source of active ingredients for health care products (3).

Plants produce an array of active ingredients that are known as secondary metabolites. Many secondary metabolites have been utilized by human beings for various purposes, specially for making medicines and as healing agents by people of Homeopathy, Allopathy, Unani - Ayurvedic medicine producers and practitioners (4).

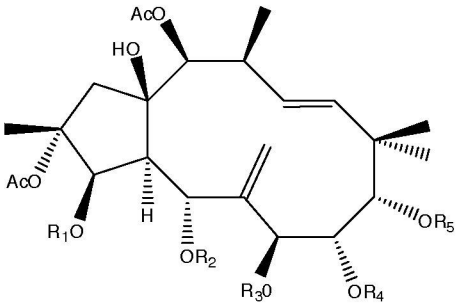
The genus *Euphorbia* is the largest in the plant family Euphorbiaceae, comprising about 2000 known species and ranging from annuals to trees. All contain latex and have unique flower structures. A significant percentage, mostly those originating in Africa and Madagascar, are succulent. 91 *Euphorbia* species are growing in Turkey (5). In this review article, we will summarize the phytochemical progress of some compounds that isolated from the genus *Euphorbia* over the past few decades. Also traditional medicine uses and biological activities of isolated compound including parts structure-activity relationships are given.

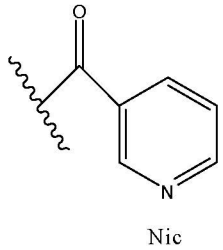
The genus *Euphorbia* contains the well-known skin irritating and tumor-promoting diterpenoids (Table 1), which have jatrophane, lathyrane and myrsinane (6), tigliane, ingenane, daphnane (7), paraliane, pepluane, segetane skeletons and sesquiterpenoids (Table 2) (euphanginol, clovandiol, euphorbioside A, euphorbioside B (8), flavonoids (Table 3) (rutin, kaempferol, myricetin, quercetin and derivatives) (9), volatile compounds (terpinene, linalool, α-terpineol, β-caryophyllene, α-humulene, germacrene-D etc.) (10), tannins (euphorbins), triterpenoids (Table 4) (lupeol, lupeol acetate, betulin, β-amyrin) and phytosterols (β-sitosterol etc.) (11). These constituents have been isolated from different parts (leaves, aerial parts, milky latex, roots and seeds) of the *Euphorbia* species.

An increasing attention has been paid to *Euphorbia* diterpenes because of their diverse structures and therapeutical importance. Macrocyclic diterpenes from *Euphorbia* species have been found to possess cytotoxic, antitumor, antibacterial, anti-inflammatory and anti-HIV activities (12). In addition, their biological activity includes antiproliferative, modulability of multidrug resistance, cytotoxic, antiviral, antidiarrheal, molluscicidal, antifeedant, antimicrobial and antipyretic-analgesic activities (7-8).

Some of the species are used in folk medicines to cure skin diseases, wounds, warts, gonorrhea, migraines and intestinal parasites in the world as well as in Turkey. *Euphorbia* genus is known to contain a wide variety of terpenoids, ranging from mono-, sesqui-, and diterpenes to triterpenoids and steroids. Many of these compounds have been investigated for their toxicity or their potential therapeutic activity, and some have been used as medicines since ancient times (13).

Table 1. Chemical structure of some diterpenoids isolated from *Euphorbia* species

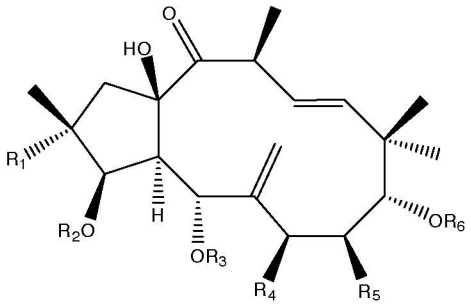


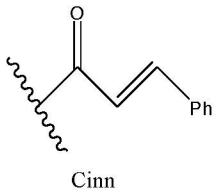


Nic

*jatrophanes

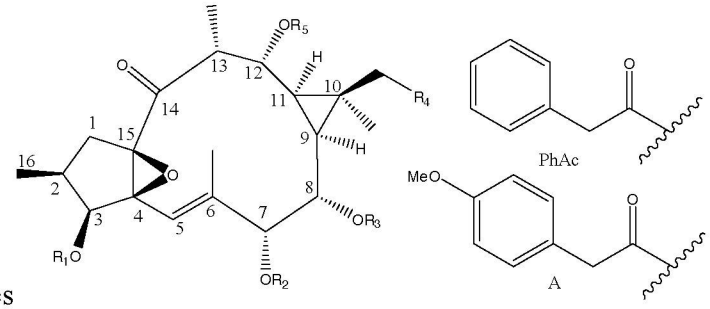
Name	R_1	R_2	R_3	R_4	R_5
2,5,14-triacetoxy-3-benzoyloxy-7-isobutyryloxy-9-nicotinoyloxy jatropha-6(17),11E-diene-8,15- diol	Bz	Ac	iBu	H	Nic
2,5,7,8,9,14-hexaacetoxy-3-benzoyloxyjatropha-6(17),11 E-dien-15-ol	Bz	Ac	Ac	Ac	Ac
2,5,9,14-tetraacetoxy-3- benzoyloxy-7-isobutyryloxyjatropha-6(17),11E-diene-8,15-diol	Bz	Ac	iBu	H	Ac
2,5,7,14-tetraacetoxy-3-benzoyloxy-9-nicotinoyloxyjatropha-6(17),11E-diene-8,15-diol	Bz	Ac	Ac	H	Nic
2,5,7,9,14-pentaacetoxy-3-benzoyloxyjatropha-6(17),11 E-diene-8,15-diol	Bz	Ac	Ac	H	Ac
Pepluanin A	Bz	Ac	Ac	Av	Nic
Pepluanin B	Bz	Ac	MeBu	H	Nic
Pepluanin C	Bz	iBu	Bz	Ac	Ac





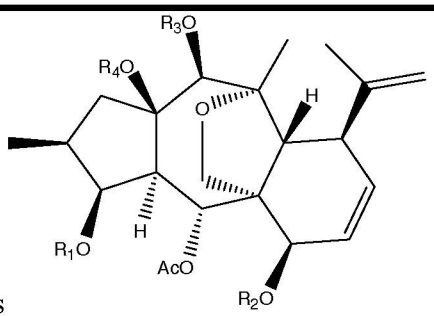
Cinn

Name	R_1	R_2	R_3	R_4	R_5	R_6
1,5,8,9-tetraacetoxy-2-benzoyloxyacetoxy-7-isobutyryloxyjatropha-6(17),11E-dien-14-	OAc	BzOAc	Ac	OiBu	OAc	Ac
5-acetoxy-3-benzoyloxy-9-cinnamoyloxy-15-hydroxyjatropha-6(17),11E-dien-14-one	H	Bz	Ac	H	H	Cinn
5-acetoxy-3,9-dicinnamoyloxy-15-hydroxyjatropha-6(17),11E-dien-14-one	H	Cinn	Ac	H	H	Cinn



*latyranes

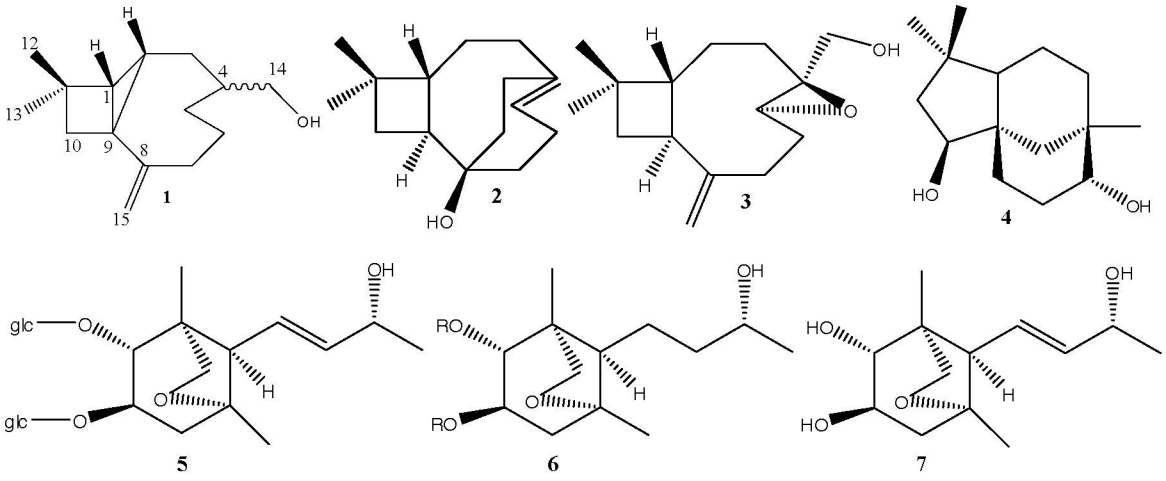
Name	R_1	R_2	R_3	R_4	R_5
3*β*,12α-diacetoxy-19-hydroxy-7α,8α-ditigloyloxyingol	Ac	Tigl	Tigl	OH	Ac
3*β*,12α-19-triacetoxy-7α-hydroxy-,8α-ditigloyloxyingol	Ac	H	Tigl	OAc	Ac
12α-19-diacetoxy-3*β*,7α-hydroxy-,8α-ditigloyloxyingol	H	H	Tigl	OAc	Ac
3*β*,8α,12α-triacetoxy-7α-isovaleryloxyingol	Ac	iVal	Ac	H	Ac
3*β*,8α,12α-triacetoxy-7α-angeloxyingol	Ac	Ang	Ac	H	Ac
3 *β*,7α,12α-triacetoxy-8α-isovaleryloxyingol	Ac	Ac	iVal	H	Ac
3 *β*,7α,12α-triacetoxy-8α-benzoyloxyingol	Ac	Ac	Bz	H	Ac
3*β*,12α-diacetoxy-8α-benzoyloxy-7α-hydroxyingol	Ac	H	Bz	H	Ac
3*β*,12α-diacetoxy-7α-benzoyloxy-8α-nicotinoyloxyingol	Ac	Bz	Nic	H	Ac
3*β*,12α,19-triacetoxy-8α-nicotinoyloxy-7α-phenylacetoxyingol	Ac	PhAc	Nic	OAc	Ac
3*β*,12α,19-triacetoxy-8α-hydroxy-7α-phenylacetoxyingol	Ac	PhAc	H	OAc	Ac



*myrsinanes

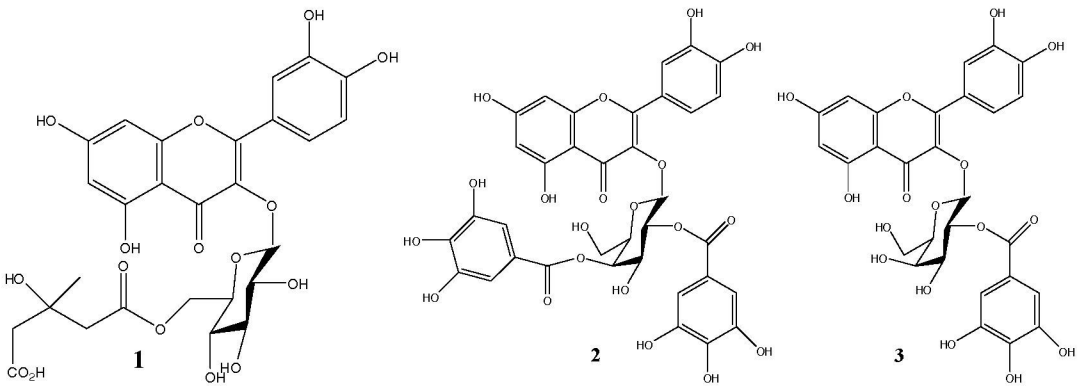
Name	R_1	R_2	R_3	R_4
5α,15*β*-di-*O*-acetyl-7*β*,14*β*-di-*O*-nicotinoyl-14-desoxo-3*β*-*O*-propanoylmyrsinol	Pr	Nic	Nic	Ac
3*β*,5α,15*β*-tri-*O*-acetyl-7*β*,14*β*-di-*O*-nicotinoyl-14-desoxomyrsinol	Ac	Nic	Nic	Ac
3*β*,5α,15*β*-tri-*O*-acetyl-7*β*-*O*-benzoyl-14*β*-*O*-nicotinoyl-14-desoxomyrsinol	Ac	Bz	Nic	Ac
5α,15*β*-di-*O*-acetyl-7*β*-*O*-benzoyl-14*β*-*O*-nicotinoyl-14-desoxo-3*β*-*O*-propanoylmyrsinol	Pr	Bz	Nic	Ac
5α, 14*β*,15*β*-tri-*O*-acetyl-7*β*-*O*-benzoyl-14-desoxo-3*β*-*O*-propanoylmyrsinol	Pr	Bz	Ac	Ac
5α, 14*β*,15*β*-tri-*O*-acetyl-7*β*-*O*-nicotinoyl-14-desoxo-3*β*-*O*-propanoylmyrsinol	Pr	Nic	Ac	Ac
5α, 14*β*-di-*O*-acetyl-15*β*-hydroxy-7*β*-*O*-nicotinoyl-14-desoxo-3*β*-*O*-propanoylmyrsinol	Pr	Nic	Ac	H

Table 2. Chemical structure of some sesquiterpenoids isolated from *Euphorbia* species



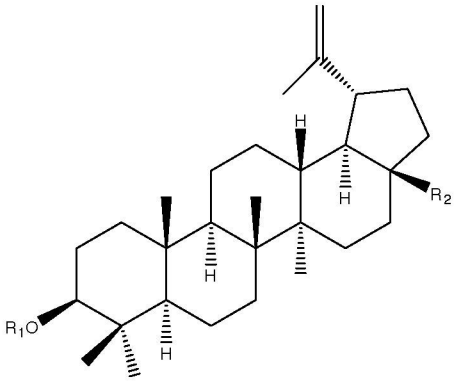
	Name
1	euphanginol
2	cyclocaryophylla-4-en-8-ol
3	4*β*,5α-epoxy-4,5-dihydrocaryophyllen-14-ol
4	clovandiol
5	euphorbioside A
6	euphorbioside B
7	deglucosyl euphorbioside A

Table 3. Chemical structure of some flavonoids isolated from *Euphorbia* species

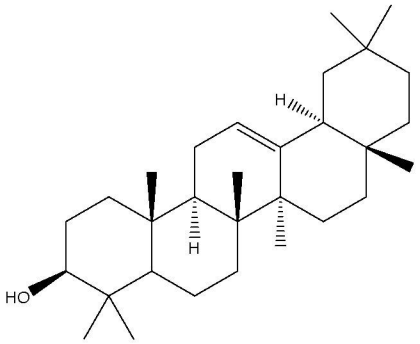


	Name
1	quercetin 3-O-6′-(3-hydroxy-3-methylglutaryl)-*β*-D-glucopyranoside
2	quercetin 3-O-(2″,3″-digalloyl)-*β*-D-galactopyranoside
3	quercetin 3-O-(2″-galloyl)-*β*-D-galactopyranoside

Table 4. Chemical structure of some triterpenoids isolated from *Euphorbia* species



Name	R_1	R_2
Lupeol acetate	Ac	Me
Betulin	H	CH_2OH
Betulinic acid	H	COOH
Lupeol	H	Me



β-amyrin

Turkey is one of the richest countries in the world in terms of plant diversity. To date approximately 10.500 plant species have been identified within its borders and 30% of these are endemic (1). The ratio of endemism is one of the most important indicators to evaluate environmental value of an area. In Turkey, the rate of endemism in plant species is relatively high when compared with other European countries (2).

The western part of Anatolia, which lies between the Aegean Sea and Central Anatolia, is called West Anatolia. In the coastal regions a typical Mediterranean climate prevails, but in the inner regions the climate favors steppe formation. There are fertile agricultural areas along the broad rivers that meanders through the valleys, but the south-western and the inner regions bordering Central Anatolia are mountainous. The mild and humid climate produces a rich flora in West Anatolia (14).

East Anatolia is the largest geographical region in Turkey. Since the area is surrounded by coastal mountain ranges, it is shielded from the moderating effect of the sea breeze. For this reason, winters are usually cold and long, and precipitation generally occurs as snow which lasts for several months. After a very short and rainy spring, a hot and dry summer follows (15).

North and South Anatolia by the Black Sea and the Mediterranean Sea shows different characteristics of topography, socio-economic welfare and ethnic origin, when compared to the other sections of the country (16).

The middle part of the Anatolian peninsula is surrounded by mountain ranges and called is "Central Anatolia". Due to shielding from the moderating effects of the sea breezes by the surrounding coastline mountains, this area is subject to cold winters and dry, hot summers. The rainfall mostly occurs in spring. The flora is mainly of the steppe character, with natural pastures, scattered and disturbed forests (17).

Traditional medicine with Euphorbia species in Turkey

In the course of history Anatolian cultures had a great impact on the constitution and development of contemporary cultures from religions to medicine. The relationship between humans and plants have existed since the existence of human beings. Due to its strategic importance, the region has been dominated during history by Western (Greeks, Romans) or Eastern (Turks, Mongolians) civilizations. These historical events have probably had a great influence on the local cultures including the

traditional and folk medicines of the communities in the region. In this part of the world, plants have been used as a source of medicines from ancient times onward. In spite of such a rich cultural heritage and relatively rich flora, the number of scientific ethnobotanical field surveys, at least published in the international journals, among the regional communities is very low. Meanwhile, the worldwide threatening factors on the traditional heritages have been valid for the region and this wealth of information has slowly vanished with the influencing factors of modernization; urbanization, migrations, development of roads and communication media, easier access to modern medicine and drugs, etc. (18).

Turkey has a great history of folk medicine. Medical folklore researches about diseases in which herbal drugs are used colloquially in Turkey, their effects and names have been going on increasingly since Republican. Historical records show that a great number of herbal drugs were exported at the time of the Ottoman Empire. For centuries, Turkish people have been using herbal medicine for the treatment of some daily diseases. In recent years, the plants – used traditionally for curative purposes – have attracted attention of the researchers. Documentation of the indigenous knowledge through ethnobotanical studies is important for the conservation and utilization of biological resources. Therefore, establishment of the local names and the indigenous uses of the plants has significant potential biocultural benefits (2). In different regions of Turkey some *Euphorbia* species have been using to treat some diseases. Different *Euphorbia* species, local names, parts used and therapeutic uses have been shown in Table 5.

Biological Activities

Anti-inflammatory activity

Inflammatory diseases are among the most common health problems treated with traditional remedies. Therefore, it is crucial to evaluate the potential of herbal remedies for the discovery of novel bioactive compounds that might serve as leads for the development of potent drugs (23).

As leucocytes play an important role in the development of the inflammatory reaction, inhibition of their migration accounts for the inflammation inhibitory effect. The water soluble fraction of *Euphorbia royleana* latex, showed dose-dependent anti-inflammatory and antiarthritic effects in different acute and chronic test models in rats and mice. It reduced the exudate volume and the migration of leukocytes and showed poor inhibitory effect on the granuloma formation induced by cotton pellets, while it had a low ulcerogenic score. The oral LD_{50} was more than 1500 mg/kg in both of rats and mice (24).

Table 5. List of plants used as a remedy in different regions of Turkey

Scientific name	Local name	Plant part used	Therapeutic uses	References
E. myrsinites L.	Sütleğen	Latex	Anthelmintic	2-19
E. rigida Bieb.	Sütleğen	Latex	Anthelmintic, antihaemorrhoidal	19
E. macroclada Boiss.	Sütlüceot, Sütleğen, Sütlüot	Latex	Antipyretic in malaria, antihaemorrhoidal, warts, wound healing, snake-scorpion bites, analgesic in toothache, wound healing, scorpion bites, eczema, fungal infection	4-20-21
E. seguieriana Necker	Tasmaotu, Sütlüot	Latex	Antipyretic in malaria, anti-inflammatory, wound healing	4-16
E. apios L.	Sürgenotu	Root	Laxative	2
E. stricta L.	Sütleğen	Latex	Analgesic in toothache, callus	1
E. agraria Bieb.	Süt otu	Latex		4
E. armena Prokh.	Sütlübiyan	Latex	Wound healing, constipation	4
E. falcata L. supsp. *falcata* var. *falcata*	Sütleğen	Latex	Eczema, fungal infection	4
E. heteradena Jaub. & Spach.	Sütleğen	Latex	Constipation	4
E. nicaeensis All. subsp. *lasiocarpa* Boiss.	Sütlüyen	Latex	Anthelmintic, antifungal	4-22
E. virgata Waldst. & Kit.	Sütcan	Flower	Eczema	4
E. coniosperma Boiss.	Sütleğen, Sütlük	Latex, Aerial parts	Wound healing, snake-scorpion bites, warts	17
Euphorbia sp.	Keringan	Latex, Stem	Constipation	15

In carrageenan-induced oedema test in rats and mice, ethyl acetate extract of *E. royleana* latex (EA) showed significant inhibition of oedema. The higher dose tested (200 mg/kg) showed 35.9% inhibition in rats and 33.3% in mice and was statistically highly significant. In the subacute test of formaldehyde included arthritis the extract showed inhibition of 39.1% and 47.8% at 100 and 200 mg/kg respectively on day 10. The extract also showed an inhibitory effect on oedema induced by formaldehyde after 4 h in a dose related manner. EA lowered the arthritis induced increase in the total leucocyte count and also showed inhibition of erythrocyte sedimentation rate, the increase of which is a common feature in arthritic conditions EA showed an inhibitory effect on the migration of leucocytes and significantly reduced the exudates volume in the pleural cavity of rats in carrageenan and dextran-induced pleurisy test. The reduction in the pleural exudate volume show the inhibitory action of EA on vascular permeability, the increase of which is a characteristic of inflammation (25).

Nitric oxide (NO), produced by inducible NO synthase (iNOS), is one of the important mediators of inflammation and excessive NO would produce detrimental effects to individuals with chronic inflammation. An inhibitory effect with a great potency and specificity on the LPS-induced NO production was observed by *Euphorbia hirta* L., with its β-amyrin component contributing to this inhibitory effect. A 95% ethanolic extract of *Euphorbia hirta* (0.1 mg/mL) or β-amyrin (0.025 mg/mL; 58 nM) abolished most of the NO production (26).

Macrophages appear to be the main cellular source of NO because these cells contribute significantly to inducible NO synthetase (iNOS) induction after lipopolysacharide (LPS) incubation. Activation of macrophages also leads to cyclooxygenase 2 (COX-2) over-production, which plays a key role in the pathogenesis of the inflammation process. Topical application of tirucallol isolated from *E. lactea* latex in TPA-induced ear oedema test in mice significantly reduced MPO (myeloperoxidase) levels in ear homogenates, indicating that a control on leucocyte migration participates in the observed topical anti-inflammatory activity. Tirucallol potently inhibited nitrite over production from LPS-stimulated peritoneal macrophages without any indication of citotoxicity. Tirucallol at 100 μM caused complete inhibition of the LPS-induced iNOS expression (100%). This effect was found similar to dexamethasone (10 μM) (27).

The triterpene alcohols and a sterol glucoside isolated from the dichloromethane extract of *E. kansui* showed inhibitory effects on TPA-induced inflammation in mice. 50% inhibitory dose is 0.2-1 mg/ear. Euphol was the most predominant triterpene alcohol constituent and 24-methylene cyclo artanol exhibited the strongest inhibitory effect (0.2 mg/ear) (28).

The alcoholic extract of *E. heyneana* at the doses of 200, 400 and 800 mg/kg exhibited significant ($P<0.05$-0.001) percentage inhibition of paw oedema at 3 hour after carrageenan injection ranging from 35.3%, 45.6%, to 47.1% compared to control group. The standard drug indomethacin at 5 mg/kg dose showed maximum percentage of inhibition of paw oedema 54.1% and among the three doses, 800 mg/kg dose showed maximum percentage inhibition of maximal paw oedema (47.1%) (29).

Antipyretic-analgesic activity

Myrsinane, isolated from *E. decipens* as whole plant chloroform extract, showed significant analgesic activity when administered to mice at dose of 5-20 mg/kg i.p. This activity is comparable to that of 100 mg/kg of aspirin or ibuprofen (30).

Resiniferatoxin, an ultrapotent capsaicin analog present in the latex of *E. resinifera*, interacts at a specific membrane recognition site, expressed by primary sensory neurons mediating pain perception as well as neurogenic inflammation. Desensitization to resiniferatoxin is a promising approach to mitigate neuropathic pain and other pathological conditions in which sensory neuropeptides released from capsaicin sensitive neurons play a crucial role (8).

Prostratin, obtained in *E. fischeriana*, showed significant analgesic and sedative activities. The 92% and 62% inhibitions were observed in sedative experiments with 20 mg/kg (p.o.) and 1 mg/kg (s.c.) in mice, respectively (31).

The ethyl acetate fraction from the residue of an 85% ethanol extract of the latex of *E. royleana* showed a dose related peripheral analgesic effect. The same fraction exhibited a significant antipyretic effect in hyperthermic rats and rabbits. The oral LD_{50} was found more than 2 g/kg in rats and mice (8).

In another study an identified use of the plant as analgesic in traditional medicine, the hexane, chloroform and ethyl acetate extracts of *E. heterophylla* root were tested for antinociceptive activity in rats. All extracts showed significant effects at doses of 150/300 mg/kg (32).

Anticancer activity

Cancer is the second most common cause of morbidity and mortality in the world, and is expected to rise in the coming decades. For solid tumors, the conventional treatments include chemotherapy, radiation therapy, and surgery. In recent years, the mechanism of cancer development strongly suggests that cancer is a systemic disease. Despite the tremendous progress made over the past few decades towards understanding the molecular biology of cancer, the disease has not been fully controlled. Relying solely on local treatment such as surgical excision or radiation therapy makes it difficult to cure or prevent tumor recurrence and metastasis. By far, chemotherapy is the most promising and commonly used treatment to reduce the risk of cancer. Nevertheless, developing new synthetic drugs can be costly and it is also difficult to screen the effective anticancer drugs from large numbers of chemical compounds. Therefore, the quest for safe and effective anticancer drugs from natural plants has become an important aspect of anticancer research.

Human hepatocellular carcinoma cell lines SMMC-7721, BEL-7402, HepG2, gastric carcinoma cell line SGC-7901 and colorectal cancer cell line SW480 were used to investigate the antiproliferative

effects of petroleum ether extract (PEE), chloroform extract (CE), ethylacetate extract (EAE), and n-butanol extract (NBE) of *Euphorbia helioscopia* L. EAE and CE could inhibit the proliferation of all five human cancer cell lines in a dose- and time-dependent manner at the concentration range of 50–200 μg/mL (33).

In 1993, Yang showed that ethylacetate and aqueous extracts of *E. fischeriana* were found to inhibit the growth of Lewis lung carcinoma and ascetic hepatoma in mice. Che *et al.*, 1999 showed antitumour effects of jolkinolides A and B isolated from *E. fischeriana* against mice bearing sarcoma and hepatocellular carcinoma at 1 mg/mL concentration. Liu *et al.* found that jolkinolide B exhibited the most potent antiproliferative activity (IC_{50} of 12.5 μg/mL=40 μM) and it inhibits DNA synthesis by down-regulating bromodeoxyuridine incorporation in LNCaP cells in a dose-dependent manner. Jolkinolide B at concentrations up to 25 μg/mL, induced G_1 arrest and neuroendocrine differentiation of LNCaP cells. On the basis of these data jolkinolide B seems to play a role in the regulation of proliferation, differentiation and apoptosis of LNCaP cells (34).

In 1997, Xu *et al.* reported that yuexiandajisu B from *E. ebracteolata* inhibited proliferation of B lymphocytes *in vitro* preliminary bioassays (35). Valente *et al.* reported the *in vitro* effect of pubescenol, helioscopinolide A, helioscopinolide B, and pubescene D isolated from *E. pubescens* on the human tumor cell lines MCF-7 (breast adenocarcinoma), NCI-H460 (nonsmall cell lung cancer), and SF-268 (CNS cancer). All compounds were found that they were moderate inhibitors of the growth of these cell lines (36). In 2005, Nishimura *et al.* reported the proliferation activity of acetone extract of the whole plants of *E. lunulata* for insulin- and interleukin-10(IL-10)-dependent cell lines. Fractionation of the active extract led to the isolation of quercetin 3-*O*-(2′,3′-digalloyl)-*β*-D-galactopyranoside, quercetin 3-*O*-(2′-galloyl)-*β*-D-galactopyranoside, quercetin, and gallic acid. Compounds showed proliferation activity for BAF/InsR (insulin-dependent cell line), whereas quercetin and gallic acid showed the strongest proliferation activity for BAF/IL 10R (37).

Ravikanth *et al.*, reported that lathyrane diterpenoids, isolated from *E. nivulia*, showed significant cytotoxic activity against Colo 205, MT2, and CEM cell lines. The LD_{50} values were almost the same in the three cell lines for the three compounds (8). 17-Acetoxy jolkinolide B and 13-hexadecanoyloxy-12-deoxyphorbol, obtained from the dried roots of *Euphorbia fischeriana*, exhibited potent cytotoxic activity to Ramos B cells with IC_{50} values of 0.023 and 0.0051 μg/mL, respectively (38). Daphnane diterpenoids and tigliane diterpenoids, isolated from the bioactivity guided fractionation of the latex of *E. poisonii*, showed strong cytotoxic selectivity for the human kidney carcinoma (A-498) cell line with potencies exceeding that of adriamycin by 10.000 times (39).

Antioxidant activity

Samples of leaves, stems, flowers and roots from *E. hirta* were tested for total phenolic content, flavonoids content and *in vitro* antioxidant activity by diphenyl-1-picrylhydrazyl (DPPH) assay. Also reducing power was measured using cyanoferrate method. The leaves extract exhibited a maximum DPPH scavenging activity of 72.96% followed by the flowers, roots and stems whose scavenging activities were 52.45%; 48.59% and 44.42% respectively. Where as the standart butylated hydroxytoluene (BHT) was 75.13% (40).

The alcoholic extract of *E. heyneana* produced dose dependent inhibition of superoxide radicals ranging from 43.17% to 91.22%. The mean (inhibition concentration) IC_{50} values for superoxide radical by alcoholic extract of *E. heyneana* and ascorbic acid were found to be 68.11 and 62.27 μg, respectively. The alcoholic extract of *E. heyneana* produced dose dependent inhibition of hydroxyl radicals ranging from 32.54% to 78.34%. The alcoholic extract of *E. heyneana* produced dose dependent inhibition of DPPH radicals ranging from 46.12% to 91.03%. The mean IC_{50} values for hydroxyl radical by alcoholic extract of *E. heyneana* and ascorbic acid were found to be 67.55 and 55.24 μg, respectively (29).

The antioxidant activity of the ethanol, acetone and petroleum ether extracts of *E. acanthothamnos* Heldr., *E. macroclada* Boiss. and *E. rigida* Bieb. were compared. *E. acanthothamnos* extract was the most active extract in all tests. The phenolic content of all extracts of *E. acanthothamnos* have shown higher phenolic content than the other extracts, the highest was found as ethanol extract. The acetone extract of *E. macroclada* demonstrated the highest flavonoid content. The antioxidant activity the ethanol extract of *E. acanthothamnos* showed the same activity as

α-tocopherol. All tested extracts of *E. macroclada* showed higher antioxidant activity than BHT and α-tocopherol. In the DPPH assay, the ethanol extract of *E. acanthothamnos* was found to be the most active extract (41).

The aerial parts of *E. petiolata* were extracted successively with n-hexane, dichloromethane and methanol. The methanol extract had significant DPPH scavenging activity. Polar compounds all exhibited considerable levels of free radical scavenging activity in DPPH assay. Kaempferol, quercetin and myricetin derivatives were the most active principles in methanol extract (42).

Antimicrobial activity

Ent-11-hydroxyabieta-8(14),13(15)-dien-16,12*β*-olide showed moderate to strong growth inhibition against *Bacillus cereus*, *B. subtilis*, *Micrococcus flavas*, *Moraxella catarrhalis*, *Neisseria sicca*, and *Candida albicans* CBS 5763 at 12.5 μg/mL concentration. Jolkinolide A also moderately inhibited the growth of *M. catarrhalis* at 50 μg/mL concentration (43). Helioscopinolide A and helioscopinolide B showed significant activity against *Staphylococcus aureus* 6538P (2.5 μg/spot) (36).

A mixture of cerebrosides from *E. peplus* showed a synergistic antifungal activity against *Candida* spp. and *Cryptococcus neoformans* strain. Moreover, 1-*O*-(*β*-D-glucopyranosyl) (2S,3S,4R,8Z)-2N-[(2′R)-20-hydroxytetracosanoil]-8-(Z)-octadecene-1,3,4-triol showed an interesting antitubercular activity with MIC of 40 μg/mL on reference strain and on two clinical isolates and a MIC of 80 μg/mL against clinical strain *M. tuberculosis* (44).

Natarajan *et al*. investigated researched the antibacterial activity of *E. fusiformis* against pathogenic strains of Gram positive (*Bacillus subtilis* and *S. aureus*) and Gram negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella typhii* A, and *S. typhii* B). Different extracts differed by their antibacterial properties significantly. The methanolic extract was found very effective, this followed by acetone and chloroform extracts. Aqueous and ethanolic extracts showed very least activity. Root stock extracts had better antibacterial properties than leaf extracts. The results of this study supported the use of this plant in traditional medicine to treat fever, wound infections and intestinal disorders (45).

The ethanolic extracts of aerial parts of *E. hirta* exhibited a broad spectrum of antimicrobial activity against *E. coli*, *P. vulgaris*, *P. aeruginosa* and *S. aureus* (46). Hydroxyparalian derivatives, isolated from *E. paralias*, showed a moderate antiviral activity (EC_{50}=14 mg/mL) against HIV-1 replication. The activity was based on the inhibition of virus induced cytopathicity in MT-4 cells (47). *Euphorbia characias* latex showed antifungal activity against *Candida albicans*. The determination of MIC 80% by macrobroth dilution method showed an antifungal activity at 159 μg/mL latex protein (48).

The MIC of the *E. helioscopia* against *B. cereus* was determined. The MIC for Soxhlet and macerated extracts were 1.25 and 0.5 mg/mL, respectively. The bioactive components some derived polyphenolic compounds such as polysaccharides, lignins and flavonoids were reported to act principally by binding to the protein coat and thus arrest absorption for the virus. Two different extraction protocols were used to test the effect of heat and solvent on the antiviral constituents of *E. helioscopia*. The results showed that the macerated extract had a higher activity in reduction of the number of plaques suggesting that the heat used in Soxhlet method might destroy the active constituents of the extract (49).

Molluscicidal and antifeedant activities

In 2001 and 2002, Abdelgaleil *et al*. reported the molluscicidal and antifeedant activities of diterpenoids from *E. paralias*. Diterpenic compounds had high molluscicidal activities on *Biomphalaria alexandrina* (snail). Antifeedant activity was tested by a conventional leafdisk method against third-instar larvae of *Spodoptera littoralis*. Compounds showed good insect antifeedants with 66.8 to 45.8% antifeedant activity (1000 mg/mL). Kansenonol was found moderately active at 500 ppm (47-50).

The aqueous and serially purified latex extracts of plants *E. pulcherima* and *E. hirta* had potent molluscicidal activity. Sublethal doses (40 and 80% of LC_{50}) of aqueous and partially purified latex extracts of both plants also significantly altered the levels of total protein, total free amino acid, nucleic acid (DNA and RNA). Also the activity of enzyme protease, acid and alkaline phosphatase

was significantly increased by various tissue of the snail *Lymnaea acuminata* in time and dose dependent manner (8).

Clinical trials

In a clinical study, the effectiveness of *E. peplus* sap in a phase I-II clinical study for the topical treatment of basal cell carcinomas (BCC), squamous cell carcinomas (SCC) and intraepidermal carcinomas (IEC) were investigated. Thirty-six patients, who had refused, failed or were unsuitable for conventional treatment, were enrolled in a phase I-II clinical study. A total of 48 skin cancer lesions were treated topically with 100–300 μL of *E. peplus* sap once daily for 3 days. The complete clinical response rates at 1 month were 82% (n = 28) for BCC, 94% (n = 16) for IEC and 75% (n = 4) for SCC. After a mean follow-up of 15 months these rates were 57%, 75% and 50%, respectively. For superficial lesions < 16 mm, the response rates after follow-up were 100% for IEC (n = 10) and 78% for BCC (n = 9). The clinical responses for these relatively unfavourable lesions (43% had failed in previous treatments, 35% were situated in the head and neck region and 30% were > 2 cm in diameter), are comparable with existing nonsurgical treatments. An active ingredient of *E. peplus* sap has been identified as ingenol mebutate (51).

Haemorrhoidal disease is a common entity in the general population and usually associated with bleeding. Surgical techniques available for the treatment are associated with discomfort, hospital stay and some complications. There is need for effective pharmacological treatment of bleeding haemorrhoids. In a prospective open label, single arm, post marketing study, a total of 1836 patients of bleeding haemorrhoids were given *Euphorbia prostrata* dry extract 100 mg tablets for 14 days. Their symptoms like bleeding, pain and congestion were assessed during and at the end of the study. Results of the study showed that bleeding was reported by 71 patiens (3.9%) as compared to 1640 (89.3%) at the beginning of the study. Pain was reported by 86 patients (4.7%) as compared to 1470 (80.1%) at the beginning of the study. Swelling was reported by 114 patients (6.2%) as compared to 1109 (60.4%) at the beginning of the study. Congestion was reported by 77 patients (4.2%) as compared to 879 (47.9%) at the beginning of the study. *Euphorbia prostrata* dry extract 100 mg tablets, given for 14 days in bleeding haemorrhoids patients showed maximum improvement during first 3 days of therapy and achieved total improvement in significant number of patients at the end of therapy (52).

In another study conducted by Arora *et al.*, a total of 125 patients with first and second degree haemorrhoids were enrolled in a 10-day trial to determine the optimal dose, efficacy, safety and tolerability of the capsule formulation (50 mg and 100 mg) of *Euphorbia prostrata* extract. The reduction in signs and symptoms of acute haemorrhoidal attack (bleeding, anal discomfort, anal discharge, pain at prolapse and proctitis) at day 10 was found to be significantly greater with 50 mg or 100 mg capsules as compared to placebo (52).

From data on file, Panacea Biotec Ltd. India, a phase III trial across India evaluated the efficacy of *Euphorbia prostrata* dry extract (100 mg tablets) in the treatment of internal haemorrhoids in first and second degree haemorrhoids. A total of 120 patients were enrolled in the trial and their rectal bleeding was stopped at the 14^{th} day. There was a statistically ($p < 0.001$) and clinically significant improvement in cessation of bleeding from the baseline to the end of the therapy (52).

E. prostrata dry extract was patented by an Indian company. The extract is patented in all major countries across the globe including: United States: US 5858371, Europe: EP 868914, Australia: AU 698407.

CONCLUSION

The genus *Euphorbia* is widespread all over the world. The diterpenoids with jatrophane, lathyrane, tigliane, ingenane, and myrsinane skeletons are among the most studied diterpenoids isolated from *Euphorbia* plants. Other types of diterpenoids, such as segetane, paraliane, pepluane, euphoractine, and casbane, along with triterpenes, sesquiterpenoids, steroids, and flavonoids are also important components. The rare compounds are cerebrosides, ellagitannin, neolignan, and manoyloxide, which isolated from *E. characias*, *E. jolkinii*, *E. quinquecostata*, and *E.segetalis*, respectively. Also, several enzymes have been isolated from the *Euphorbiaceae* family. The biological research on *Euphorbia*

species has supported the use of some plants in traditional medicines or revealed the new activities on modern pharmacological levels. The observed biological activities include mainly anti-inflammatory activity, antipyretic-analgesic activity, anticancer activity, antioxidant, antimicrobial activity, molluscicidal and antifeedant activities. The insight of structure-activity relationships study on diterpenoids has given us more detailed information about the active core framework and substituents (8).

Ethnobotanical studies are the first and the most important steps to evaluate and elucidate the plants. The investigations on plants and their active compounds take a great interest in traditional medicine. After pharmacological and toxicological studies, there will be a possibility to be used in therapy. Turkey has a great history of folk medicine, but this knowledge has not been documented extensively so far. There were only a few methodical studies of traditional medicine and the utilization of some plants were mentioned without citing any region in an encyclopaedic book in Turkey before nearly 20 years ago. In the recent years researchers have carried out many studies about traditional medicine in Turkey. Now we have important informations, documents and great opportunities to study on medicinal plants. Some *Euphorbia* species have been studied for years, but many more species are waiting to work on them. In the present review we have explored to the some details of the Euphorbia species information, their habitat, ethnobotany, ethnopharmacology, traditional and modern uses.

REFERENCES

1. Kargıoğlu M, Cenkci S, Serteser A, Evliyaoğlu N, Konuk M, Kök MŞ, Bağcı Y, An ethnobotanical survey of Inner-West Anatolia, Turkey, Hum Ecol 36, 763-777, 2008.
2. Polat R, Satıl F, An ethnobotanical survey of medicinal plants in Edremit Gulf (Balıkesir–Turkey), J Ethnopharmacol 139, 626-641, 2012.
3. Dey M, Ripoli C, Pouleva R, Dorn R, Aranovich I, Zaurov D, Kurmukov A, Eliseyeva M, Belolipov I, Akimaliev A, Sodombekov I, Akimaliev D, Lila MA, Raskin I, Plant extracts from Central Asia showing antiinflammatory activities in gene expression assays, Phytother Res 22, 929-934, 2008.
4. Altundağ E, Öztürk M, Ethnomedicinal studies on the plant resources of East Anatolia, Turkey, Procedia Soc Behav Sci 19, 756-777, 2011.
5. Davis PH, Flora of Turkey and the East Aegean Islands, 7, pp.571, Edinburgh University Press, Edinburgh, 1970.
6. Sulyok E, Vasas A, Redei D, Forgo P, Kele Z, Pinke G, Hohmann J, New premyrsinane-type diterpene polyesters from *Euphorbia falcata,* Tetrahedron 67, 7289-7293, 2011.
7. Jassbi AR, Chemistry and biological activity of secondary metabolites in *Euphorbia* from Iran, Phytochemistry 67, 1977-1984, 2006.
8. Shi QW, Su XH, Kiyota H, Chemical and pharmacological research of the plants in genus *Euphorbia,* Chem Rev 108, 4295-4327, 2008.
9. Noori M, Chehreghani A, Kaveh M, Flavonoids of 17 species of *Euphorbia* (Euphorbiaceae) in Iran, Toxicol Environ Chem 91(4), 631-641, 2009.
10. Fokialakis N, Melliou E, Magiatis P, Harvala C, Mitaku S, Composition of the steam volatiles of six *Euphorbia* spp. from Greece, Flavour Frag J 18, 39-42, 2003.
11. Patil SB, Naikwade NS, Magdum CS, Review on phytochemistry and pharmacological aspects of *Euphorbia hirta* Linn., JPRHC 1(1), 113-133, 2009.
12. Demirkıran Ö, Topçu G, Hussain J, Ahmad VU, Choudhary MI, Structure elucidation of two new unusual monoterpene glycosides from *Euphorbia decipiens*, by 1D and 2D NMR experiments, Magn Reson Chem 49, 673-677, 2011.
13. Tang Q, Su Z, Han Z, Ma X, Xu D, Liang Y, Cao H, Wang X, Qu X, Hoffman A, Liu H, Gu D, Qiu D, LC–MS method for detecting prostratin in plant extracts and identification of a high-yielding population of *Euphorbia fischeriana*, Phytochem Lett 5, 214-218, 2012.
14. Honda G, Yeşilada E, Tabata M, Sezik E, Fujita T, Takeda Y, Takaishi Y, Tanaka T, Traditional medicine in Turkey VI. Folk medicine in West Anatolia: Afyon, Kütahya, Denizli, Muğla, Aydın provinces, J Ethnopharmacol 53, 75-87, 1996.

15. Tabata M, Sezik E, Honda G, Yeşilada E, Fukui H, Goto K, Ikeshiro Y, Traditional Medicine in Turkey III. Folk Medicine in East Anatolia, Van and Bitlis Provinces, Int J Pharmacog 32(1), 3-12, 1994.
16. Yeşilada E, Sezik E, Honda G, Takaishi Y, Takeda Y, Tanaka T, Traditional medicine in Turkey IX: Folk medicine in North-West Anatolia, J Ethnopharmacol 64, 195-210, 1999.
17. Sezik E, Yeşilada E, Honda G, Takaishi Y, Takeda Y, Tanaka T, Traditional medicine in Turkey X. Folk medicine in Central Anatolia, J Ethnopharmacol 75, 95-115, 2001.
18. Yeşilada E, Past and future contributions to traditional medicine in the health care system of the Middle-East, J Ethnopharmacol 100, 135-137, 2005.
19. Ezer N, Avcı K, Çerkeş (Çankırı) yöresinde kullanılan halk ilaçları, Hacettepe Üniversitesi Eczacılık Fakültesi Dergisi 24(2), 67-80, 2004.
20. Yeşil Y, Kürecik (Akçadağ/Malatya) bucağında etnobotanik bir araştırma, pp. 109-110, M. Sc. Thesis, Istanbul University Health Science Institute, İstanbul, 2007.
21. Oral DÇ, Konya ilinde kullanılan halk ilaçları üzerinde etnobotanik araştırmalar, pp. 49-50, M. Sc. Thesis, Gazi University Health Science Institute, Ankara, 2007.
22. Kültür Ş, Medicinal plants used in Kırklareli Province (Turkey), J Ethnopharmacol 111, 341-364, 2007.
23. Erdemoğlu N, Küpeli E, Yeşilada E, Anti-inflammatory and antinociceptive activity assessment of plants used as remedy in Turkish folk medicine, J Ethnopharmacol 89, 123-129, 2003.
24. Bani S, Kaul A, Jaggi BS, Suri KA, Suri OP, Sharma OP, Anti-inflammatory activity of the hydrosoluble fraction of *Euphorbia royleana* latex, Fitoterapia 71, 655-662, 2000.
25. Bani S, Chand D, Suri KA, Suri OP, Sharma OP, Antiinflammatory effects of an ethyl acetate extract of *Euphorbia royleana,* Phytother Res 10, 285-291, 1996.
26. Shih MF, Cheng YD, Shen CR, Cherng JY, A molecular pharmacology study into the anti-inflammatory actions of *Euphorbia hirta* L. on the LPS-induced RAW 264.7 cells through selective iNOS protein inhibition, J Nat Med 64, 330-335, 2010.
27. Fernandez-Arche A, Saenz MT, Arroyo M, Puerta RDL, Garcia MD, Topical anti-inflammatory effect of tirucallol, a triterpene isolated from *Euphorbia lactea* latex, Phytomedicine 17, 146-148, 2010.
28. Yasukawa K, Akihisa T, Yoshida ZY, Takido M, Inhibitory effect of euphol, a triterpene alcohol from the roots of *Euphorbia kansui*, on tumour promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin, J Pharm Pharmacol 52, 119-124, 2000.
29. Battu GR, Ethadi SR, Priya VG, Priya SK, Chandrika K, Rao VA, Reddy SO, Evaluation of antioxidant and anti-inflammatory activity of *Euphorbia heyneana* Spreng, Asian Pacific J Trop Biomed 191-194, 2011.
30. Ahmad VU, Hussain H, Bukhari IA, Hussain J, Jassbi AR, Dar A, Antinociceptive diterpene from *Euphorbia decipiens,* Fitoterapia 76, 230-232, 2005.
31. Ma QG, Liu WZ, Wu XY, Zhou TX, Qin GW, Diterpenoids from *Euphorbia fischeriana,* Phytochemistry 44(4), 663-666, 1997.
32. Vamsidhar I, Mohammed AH, Nataraj B, Rao CM, Ramesh M, Antinociceptive activity of *Euphorbia heterophylla* roots, Fitoterapia 71, 562-563, 2000.
33. Wang ZY, Liu HP, Zhang YC, Guo LQ, Li ZX, Shi XF, Anticancer potential of *Euphorbia helioscopia* L. extracts against human cancer cells, Anat Rec 295, 223-233, 2012.
34. Sun YX, Liu JC, Chemical constituents and biological activities of *Euphorbia fischeriana* Steud., Chem Biodivers 8, 1205-1214, 2011.
35. Xu ZH, Sun J, Xu RS, Qin GW, Casbane diterpenoids from *Euphorbıa ebracteolata,* Phytochemistry 49(1), 149-151, 1998.
36. Valente C, Pedro M, Duarte A, Nascimento MSJ, Abreu PM, Ferreira MJU, Bioactive diterpenoids, a new jatrophane and two ent-abietanes, and other constituents from *Euphorbia pubescens,* J Nat Prod 67, 902-904, 2004.
37. Nishimura T, Wang LY, Kusano K, Kitanaka S, Flavonoids that mimic human ligands from the whole plants of *Euphorbia lunulata,* Chem Pharm Bull 53(3), 305-308, 2005.
38. Wang YB, Huang R, Wang HB, Jin HZ, Luo LG, Qin GW, Diterpenoids from the roots of *Euphorbia fischeriana,* J Nat Prod 69, 967-970, 2006.

39. Fatope MO, Zeng L, Ohayaga JE, Shi G, McLaughlin JL, Selectively cytotoxic diterpenes from *Euphorbia poisonii,* J Med Chem 39, 1005-1008, 1996.
40. Basma AA, Zakaria Z, Latha LY, Sasidharan S, Antioxidant activity and phytochemical screening of the methanol extracts of *Euphorbia hirta* L., Asian Pac J Trop Med 386-390, 2011.
41. Barla A, Öztürk M, Kültür Ş, Öksüz S, Screening of antioxidant activity of three *Euphorbia* species from Turkey, Fitoterapia 78, 423-425, 2007.
42. Nazemiyeh H, Kazemi EM, Zare K, Jodari M, Nahar L, Sarker SD, Free radical scavengers from the aerial parts of *Euphorbia petiolata,* J Nat Prod 64, 187-190, 2010.
43. Sutthivaiyakit S, Thapsut M, Prachayasittikul V, Constituents and bioactivity of the tubers of *Euphorbia sessiliflora,* Phytochemistry 53, 947-950, 2000.
44. Cateni F, Zilic J, Falsone G, Scialino, Banfi E, New cerebrosides from *Euphorbia peplis* L.: antimicrobial activity evaluation, Bioorg Medicinal Chem Lett 13, 4345-4350, 2003.
45. Natarajan D, Britto SJ, Srinivasan K, Nagamrugan N, Mohanasundari C, Perumal G, Anti-bacterial activity of *Euphorbia fusiformis*-a rare medicinal herb, J Ethnopharmacol 102, 123-126, 2005.
46. Sudhakar M, Rao CV, Rao PM, Raju DB, Venkateswarlu Y, Antimicrobial activity of *Caesalpinia pulcherrima, Euphorbia hirta* and *Asystasia gangeticum,* Fitoterapia 77, 378-380, 2006.
47. Abdelgaleil SAM, Kassem SMI, Doe M, Baba M, Nakatani M, Diterpenoids from *Euphorbia paralias,* Phytochemistry 58, 1135-1139, 2001.
48. Giordani R, Trebaux J, Masi M, Regli P, Enhanced antifungal activity of ketoconazole by *Euphorbia characias* latex against *Candida albicans,* J Ethnopharmacol 78, 1-5, 2001.
49. Ramezani M, Behravan J, Arab M, Farzad SA, Antiviral activity of *Euphorbia helioscopia* extract, J Biol Sci 8(4), 809-813, 2008.
50. Abdelgaleil SAM, El-Aswad AF, Nakatani M, Molluscicidal and anti-feedant activities of diterpenes from *Euphorbia paralias* L., Pest Manag Sci 58, 479-482, 2002.
51. Ramsay JR, Suhrbier A, Aylward JH, Ogbourne S, Cozzi SJ, Poulsen MG, Baumann KC, Welburn P, Redlich GL, Parsons PG, The sap from *Euphorbia peplus* is effective against human nonmelanoma skin cancers, Br J Dermatol 164, 633-636, 2011.
52. Bakhshi GD, Langade DG, Desai VS, Prospective, Open label study of *Euphorbia prostrata* extract 100 mg in the treatment of bleeding haemorrhoids, Bombay Hospital Journal 50(4), 577-583, 2008.

Received: 03.05.2012
Accepted: 17.05.2012