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Composition, functional and medicinal importance of propolis: A Review

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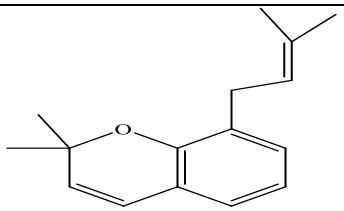
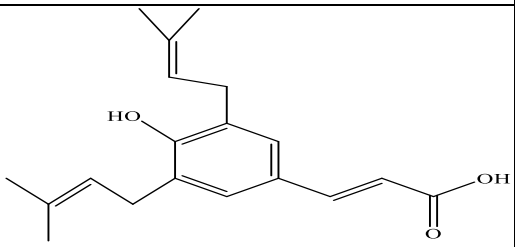
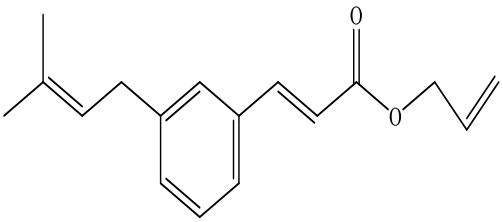
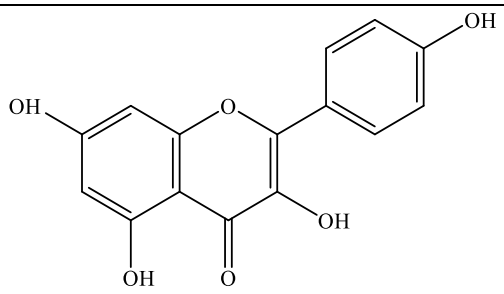
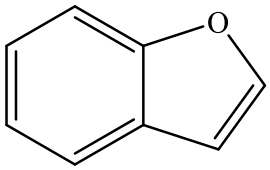
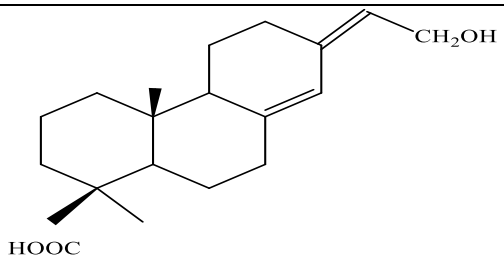
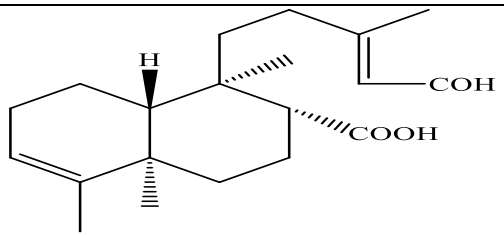
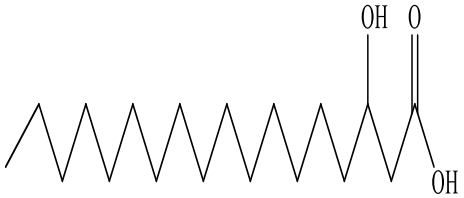
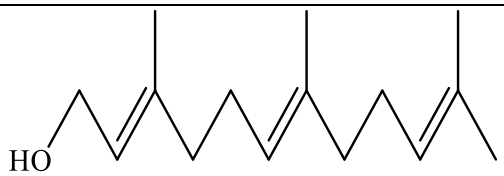
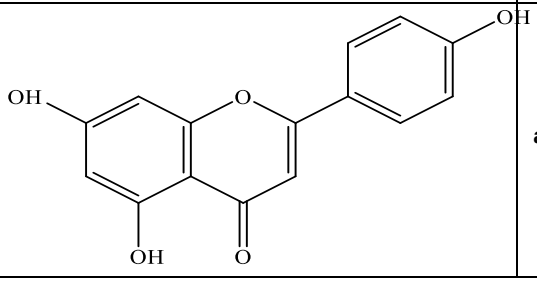
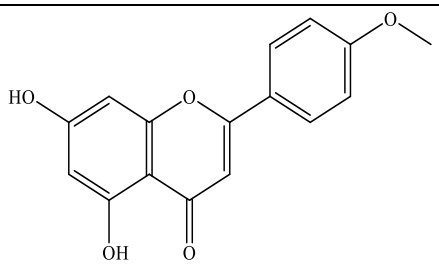
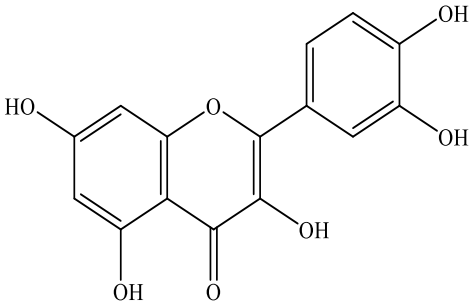
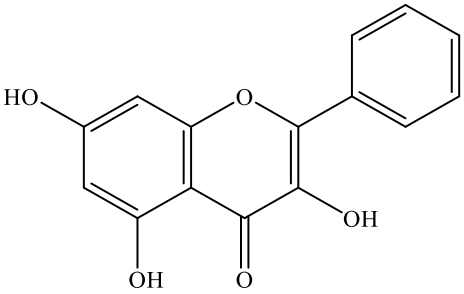
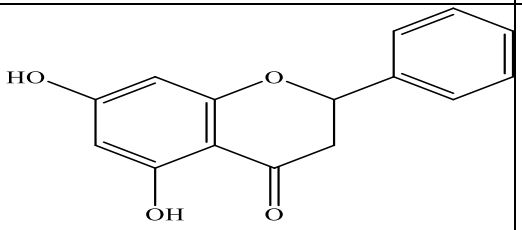
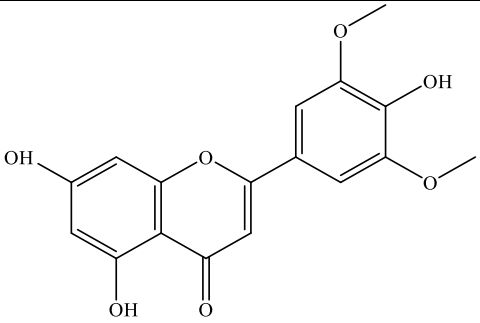
Table S1: Important bioactive compounds in propolis.

Bioactive compound in Propolis	Chemical structure	Biological activity	References
Phenolic compound: 2, 2-dimethyl-8-prenylchromene		**Antimicrobial**	**(Pasupuleti et al., 2017; Viuda Martos et al., 2008)**
Phenolic compound: 4-hydroxy-3, 5-diprenyl cinnamic acid (artepillin C)		**Antimicrobial, anti-inflammatory, anticancer**	**(Pasupuleti et al., 2017; Viuda Martos et al., 2008)**
Phenolic compound: 3-prenyl cinnamic acid allyl ester		**Antimicrobial**	**(Pasupuleti et al., 2017; Viuda Martos et al., 2008)**

Phenolic compound: kaempferide		**Antitumor, anticancer**	**(Pasupuleti et al., 2017; Viuda Martos et al., 2008)**
Phenolic compound: propolis benzofuran		**Antifungal**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Terpenoid: isocupressic acid, a labdane diterpenoid		**Antifungal**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Terpenoid:13C-symphyoreticulic acid, a clerodane diterpenoid		**Antitumor**	**(Pasupuleti et al., 2017; Viuda Martos et al., 2008**
Terpenoid: esters of long-chain fatty acids, (3-hydroxystearic acid (n = 11) procrim a; 3-hydroxystearic acid (n = 13), procrim b and a pentacyclic triterpenoid (lupeol))		**Antioxidant, antimicrobial, antitumor**	**(Huang et al., 2014; Salatino et al., 2005; Viuda Martos et al., 2008)**
Terpenoid: farnesol, a sesquiterpenoid		**Antifungal**	**(Viuda Martos et al., 2008; Cotoras et al., 2013)**
Flavonoid: apigenin		**Antibacterial, anti-inflammatory**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**

Flavonoid: acacetin		**Antiallergy, anticancer**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Flavonoid: quercetin		**Anticancer, antiallergy, antibacterial, anti-inflammatory**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Flavonoid: galangin		**Anticancer, antioxidant**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Flavonoid: pinocembrin		**Antimicrobial, anticancer**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
Flavonoid: chrysin		**Antibacterial, anti-inflammatory, anticancer**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**

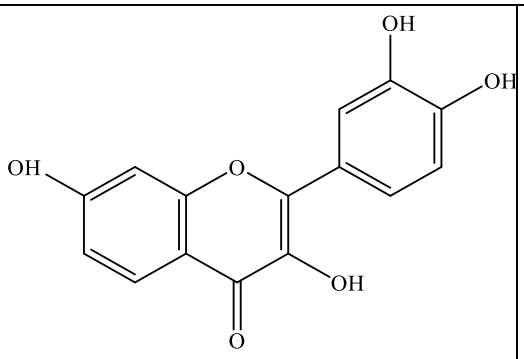
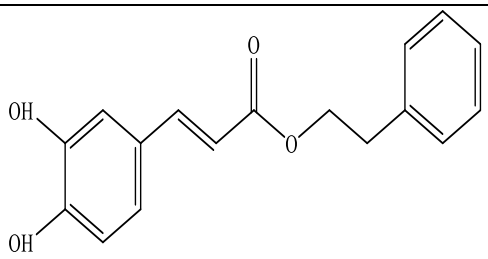
Flavonoid: fisetin		**Antibacterial, antiallergy, anticancer**	**(Viuda Martos et al., 2008; Abubakar et al., 2012)**
Flavonoid: caffeic acid phenethyl ester		**Antitumor, anticancer**	**(Viuda Martos et al., 2008; Khalil and Sulaiman, 2010)**
10-hydroxyl-2-decenoic acid		**Antibiotic, antitumor**	**(Pasupuleti et al., 2017; Izuta et al., 2009)**

Table S2: Bioactive potential of propolis from different geographic origins.

Function	Origin	Propolis type	Type of extract	Effect	Reference
Antioxidant activity	Portugal	European propolis /*Populus nigra*	Methanolic extract	Decrease in lipid peroxidation, Free radical scavenging	(Valente et al., 2011)
	Brazil	Propolis from the stingless bee/ *Melipona orbignyi*	PEE	Inhibition of hemolysis and lipid peroxidation	(Campos et al., 2015)
	Cuba	Red propolis/*C.rosea*	Methanolic extract	Free radical scavenging	(Cuesta-Rubio et al., 2002)
	Turkey	Mediterranean propolis /*Populus spp*	PEE	Decrease of DNA damage induced by H2O2, Decrease in CAT activity and MDA levels in NOS inhibited rats, Decrease in malondialdehyde	(Aliyazicioglu et al., 2007; Yonar et al., 2002)
	China	European propolis/ *Populus nigra*	Ethyl acetate extract	Free radical scavenging and ferric reducing activity	(Yang et al., 2011)
	Uruguay	European propolis and green propolis /*Populus nigra* and *B. dracunculifolia*	PEE	Inhibition of low density lipoprotein peroxidation and NADPH oxidase and increase in nitric oxide synthase	(Silva et al., 2011)
	Algeria	Mediterranean propolis/ *Populus spp.* and *Cistus spp.*	Methanolic extract	Free radical scavenging and ferric reducing activity	(Piccinelli et al., 2013)
Anti-Inflammatory activity	Croatia	European propolis /*Populus nigra*	Water soluble derivates PEE	Reduction of DNA damage in peripheral lymphocytes, Suppression of functional activity of macrophages	Oršolić et al., 2013; Oršolić et al., 2014)
	Brazil	Green propolis/*B. dracunculifolia*	PEE PWE	Inhibition of carrageenan-induced rat hind paws edema and the chemotaxis of human polymorphonuclear leukocytes (PMNs) Decrease in the number of macrophages and neutrophils; inhibition of proinflammatory cytokines and increase of anti-inflammatory cytokines	(Naito et al., 2007; Machado et al., 2012)
	Chile	European propolis /*poplar trees*	PEE	Inhibition of NO release by the macrophages	(Valenzuela-Barra et al., 2015)
	China	European propolis/ *Populus nigra*	PEE and PWE	Inhibition of the activation and differentiation of mononuclear macrophages; decrease prostaglandin-E2 (PGE 2) and nitric oxide (NO) levels	(Hu et al., 2005)
	Nepal	Nepalese propolis/ probably *Shorea robusta, Dalbergia sissoo, Acacia catechu,* and *Bombax cieba*	PEE	Inhibiting IL-6, TNF-α, and IL-13 gene expression in BMMC and also inhibiting the activation of IKK leading to NF-κBinactivation	(Jain et al., 2015)

Antitumor activity	**Thailand**	**Propolis from stingless bee/*Trigona laeviceps***	**Hexane extract**	**High antiproliferative activity against the five cancer cell lines and low cytotoxic activity on the normal cell lines**	**(Umthong et al., 2011)**
	Poland	**European propolis /*Populus nigra* and some species of *Betulaalba***	**PEE**	**Inhibition of cell growth and reduction of cell size of the tested cancer cells**	**(Kubina et al., 2015)**
	Brazil	**Red propolis/*D. ecastaphyllum***	**Methanolic extract**	**Killing 100% of PANC-1 cells in the nutrient-deprived condition Inhibition of human prostate cancer cells proliferation by regulating the protein expression of cyclin D1, B1 and cyclin dependent kinase (CDK), p21 Reduction of migration and sprouting of endothelial cells and attenuation of new blood vessels formation; decrease in the differentiation of embryonic stem cells into CD31 positive cells Inhibition of angiogenesis in N-butyl-(-4-hydroxybutyl) nitrosamine- (BBN-) induced rat bladder cancer**	**(Daleprane et al., 2012; Awale et al., 2008; Li rt al., 2007; Dornelas et al., 2017)**
		Green propolis/*B. dracunculifolia*	**PEE**		
		Red propolis/*D. ecastaphyllum*	**PEE**		
		Green propolis/*B. dracunculifolia*	**PWE**		
	Turkey	**Mediterranean propolis /*Populus spp., Eucalyptus spp.,* and *Castanea sativa***	**PEE**	**Increase of apoptosis through the caspase pathway**	**(Vatansever et al., 2010)**
	Iraq	**European propolis /*Populus nigra***	**PWE**	**Inhibition of HL-60 cells proliferation and induction of apoptosis by down regulating Bcl-2 protein and up regulating Bax; decrease of mitotic cells and increase of p53 and Ki-67 expression inHCT-116 tumor-bearing mice**	**(Sulaiman et al., 2012)**
	Iran	**European propolis /*Poplar spp. ,Ferula ovina***	**PEE**	**Decrease of tumour incidence, number of lesions, structural abnormalities, and beta-catenin and induction of proapoptotic Bax expression and reduction of antiapoptotic Bcl-2 expression**	**(Sulaiman et al., 2012)**
	China	**European propolis/ *Populus nigra***	**PEE**	**Inhibition of VEGF expression**	**(Izuta et al., 2009)**
	Korea	**European propolis /*Populus nigra***	**PEE**	**Inhibition of angiogenesis in chick embryo chorioallantoic membrane and inhibition of CPAE cells proliferation**	**(Song et al., 2002)**
	Portugal	**European propolis/ *Populus***	**Methanolic extract**	**Inhibition tumor cells growth exhibiting selective toxicity against malignant cells**	**(Valente et al., 2011)**

		nigra		**compared to normal cells**	
Immuno modulatory activity	**Brazil**	**Green propolis/*B. dracunculifolia***	**PEE** **Hydroalcoholic (HPE) solution**	**Upregulation of toll-like receptor-2 and receptor-4 expression and increases in interleukin-1 and interleukin-6 production** **Upregulation of toll-like receptor-2 and receptor-4 mRNA expression** **Stimulation of interleukin-1*β* production and inhibition of interleukin-6 and interleukin-10 productions** **Increase of H2O2 generation and decrease of NO generation** **Decrease of splenocyte proliferation and increase of IFN-*γ* production by spleen cells**	**(Orsatti et al., 2010; Sá-Nunes et al., 2003)**
	Indonesia	**The Pacific region propolis/*Macaranga tanarius* and *M. indica***	**HPE**	**Increase of IgG generation and macrophage phagocytosis activity and capacity**	**(Dewi, 2009)**
	Turkey	**Mediterranean propolis /*Populus spp., Eucalyptus spp.,* and *Castanea sativa***	**PEE**	**Suppression of neopterin release and tryptophan degradation**	**(Girgin et al., 2009)**