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Commentary

Anticancer bioactivity of compounds from medicinal plants used in European medieval traditions

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ABSTRACT

Since centuries, natural compounds from plants, animals and microorganisms were used in medicinal traditions to treat various diseases without a solid scientific basis. Recent studies have shown that plants that were used or are still used in the medieval European medicine are able to provide relief for many diseases including cancer. Here we summarize impact and effect of selected purified active natural compounds from plants used in European medieval medicinal traditions on cancer hallmarks and enabling characteristics identified by Hanahan and Weinberg. The aim of this commentary is to discuss the pharmacological effect of pure compounds originally discovered in plants with therapeutic medieval use. Whereas many reviews deal with Ayurvedic traditions and traditional Chinese medicine, to our knowledge, the molecular basis of European medieval medicinal approaches are much less documented.

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1. Introduction

From Antiquity to Modern Times, druids, healers, shamans, witches and modern medicine took advantage of natural remedies from Mother Nature to cure human diseases, as natural products provided a rich source of pharmacophores that found applications in the fields of medicine, pharmacy and biology. The knowledge about herbs, plants, flowers, leaves, tree bark, seeds, oils, or roots can be traced back over centuries from Sumerians to ancient Egyptians, Muslim, Indian, Chinese and European medieval medicines as reported in historical herbal texts [1]. European medieval herbal medicine was derived from the Romans and Greeks (Pedanius Dioscorides), which in turn was influenced by Babylonian and Egyptian medicinal plant traditions [2]. Ancient Greek medical treatises already describe theories of tumor formation and potential therapeutic methods [3]. In medieval times, Benedictine monasteries copied and translated Greek and Roman texts so that corresponding medicinal traditions became also available in Europe and England. In the 12th century, Hildegard von Bingen described tinctures, herbs and healing properties of plants in her treatises “*Causae et Curae*” and “*Liber subtilitatum diversarum naturarum creaturarum*”. Bohemian

herbalist Maria Treben collected and applied traditional German and Eastern European recipes based on the use of medicinal plant preparations including famous “Swedish bitters”, a herbal tonic containing *Aloe vera*, *Angelica*, *Carlina*, *Rheum rhabarbarum*, *Senna alexandrina* and *Curcuma zedoaria* as well as camphor, manna, myrrh, saffron and other less defined ingredients. These traditional herbal are criticized due to side effects and absence of scientific proof of concept. Nevertheless, recognition of the potential of natural products is increasing nowadays (Table 1) and appreciation of traditional medicine is growing, so that these ancestral European findings are again taken into account in the current area of new drug discovery and in large scale screening programs for the discovery of anticancer compounds [4].

So far, many reviews reported the anti-tumor potential of compounds originating from terrestrial or marine plants already used in Ayurvedic and traditional Chinese or African medicines [5–7], however the molecular basis of European traditions is much less documented [8,9] and thus deserves a critical overview. We will highlight hereafter a non-exhaustive list of compounds (Fig. 1) originally discovered in European plants with therapeutic medieval use and their currently documented molecular impact on selected cancer hallmarks (human epidermal growth factors, cell cycle machinery, immune activators, replicative immortality, invasion and metastasis, angiogenesis, cell death, aberrant metabolism and inflammation) (Table 2) in reference to Hanahan and Weinberg classification [10].

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Table 1
Medicinal indications for the use of bioactive compounds.

Plant of origin	Usual name	Clinical use or self-medication	Medical indications
<i>Matricaria chamomilla</i>	Chamomile	Herbal tea/essential oil	Stomach, irritable bowel syndrome, gentle sleep aid, mild laxative and anti-inflammatory and bactericidal
<i>Hypericum perforatum</i>	St John's wort	Photodynamic therapy Homeopathy	Cancer Depression
<i>Vitis vinifera</i>	Red grappes	Pills (Resveol [®])	Antioxidant, calories decrease
<i>Silybum marianum</i>	Blessed milk thistle Saint Mary's Thistle	Legalon [®] pills	Digestion disorders in case of acute and chronic hepatitis Cirrhosis
<i>Rosmarinus officinalis</i>	Rosemary	Herbal tea/essential oil	Blood pressure regulation, antidepressant
<i>Allium sativum</i>	Garlic	Homeopathy Garlic supplements (phytotherapy)	Chronic bronchitis High blood pressure
<i>Glycyrrhiza glabra</i> L.	Licorice	Phytotherapy pills (DGL500)	Digestion disorders
<i>Arnica montana</i>	Arnica	Homeopathy	Pain, bruises
<i>Tanacetum parthenium</i>	Feverfew	nd	nd
<i>Crocus sativus</i>	Safran	nd	nd
<i>Calendula officinalis</i>	Marigold	Homeopathy, cream (Homeoplasmin)	Pain, skin disorders
<i>Arctium lappa</i>	Greater burdock	Homeopathy	Excema, acne

2. Molecular targets of compounds from medieval plants

2.1. Human epidermal growth factor (HER)

Cancer sustains uncontrolled proliferation by enhancing growth activators and by inhibiting growth suppressors. Proliferative

signaling is enhanced by overexpression or mutation of cell surface receptors with intracellular tyrosine kinase domains such as epidermal growth factor receptors (EGFR) and human EGF receptor 2 (HER2) [11], an ubiquitous transmembrane tyrosine kinase receptor protein implicated in growth-related processes critical for development and progression of malignant tumors including

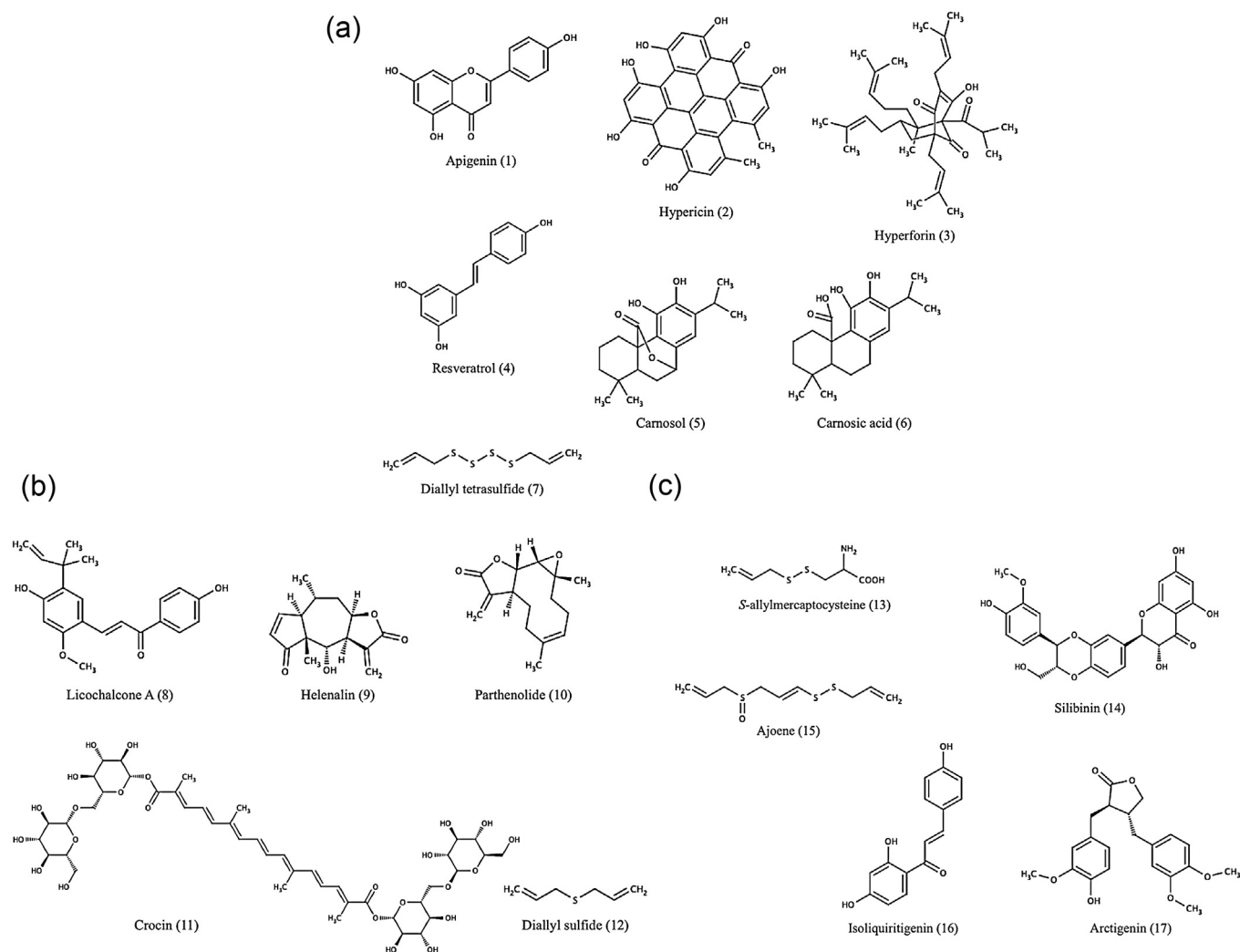


Fig. 1. (A–C) Natural compounds with anti-cancer bioactivities from medicinal plants used in European medieval traditions.

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