



## Review Article

## MAJOR GROUPS OF ANTIMICROBIAL COMPOUNDS FROM PLANTS

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### Abstract

A wide variety of secondary metabolites can be found in plant material. These metabolites have antimicrobial properties and are structurally designated as tannins, flavonoids, alkaloids as well as terpenoids. In the search for alternative treatment to bacterial infections, dietary products and healthy lifestyles, the need for validated data has become imperative. Most of these preparations are not regulated and can be purchased off the shelves. For this reason, the public should be educated in order to make informed choices. This review assists the programme in providing a summary of the structures found in many plant extracts. The effectiveness of various compounds would give an overall idea of the screening efforts of each substance, thereby enabling the public as well as practitioners' when considering treatment of a wide range of ailments. Patients' compliance to self-medicating could be effectively controlled when using "over the counter" preparations.

**Keywords:** medical plants; phenolic compounds; *flavonoids*, *tannins*; *terpenoids*; *catechin*.

### INTRODUCTION

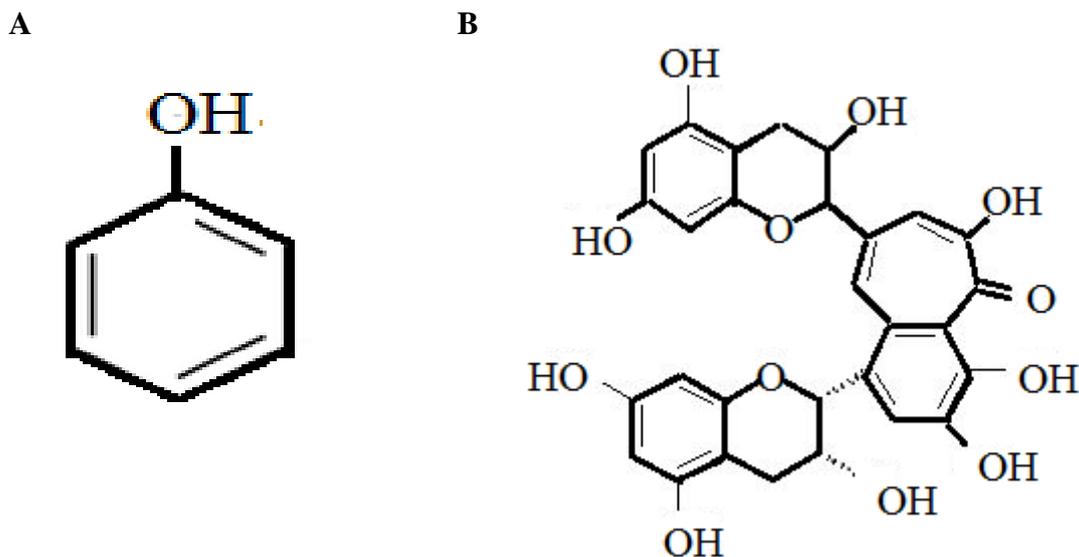
We can now locate substances of medicinal values within structural organelles of plants. With the emergence of nuclear magnetic resonance (NMR) and high performance liquid chromatography (HPLC) plant components in the form of Phytochemicals have been identified (HPLC) [1, 2, 3]. Medicinal plant extracts are used commercially for their therapeutic potential with low cytotoxicity and high effectiveness. Although the healing properties of plants lie in their chemical compositions [4], only a fraction of plant extracts has been validated scientifically for treatment of primary ailments. The most synergy is reported when a combination of oils are used in treatment of various ailments. The biological compounds identified in plant extracts require assessment of their chemical components with a specified concentration [5]. Chemical substances known as secondary metabolites produce a physiological reaction in human cells. These metabolites are utilised for cell development and growth [6]. Extract of these bioactive groups of plants are phenolic

compounds terpenoids, flavonoids, tannins and alkaloids [6,7].

### PHENOLIC COMPOUNDS

A wide range of plant substances which have *phenolic* compound possess aromatic rings bearing one or more hydroxyl substitutes [8]. Located in the cell vacuole of plant cells, these water-soluble extracts, most frequently occur combined with sugar as glycosides. Among the natural *phenolic* compounds, *flavonoids* form the largest group, however, simple monocyclic *phenols*, *phenol propanoids* and *phenolic quinines* all exist in considerable numbers [8]. In many cases, these substances serve as defence mechanisms of plants against microorganisms, insects and herbivores [7]. Some substances, such as *terpenoids*, give plants their odours. Others such as *tannins* and *quinines* are responsible for plant pigment whilst aromatic compounds such as phenols are responsible for plant flavour. Useful antimicrobial phytochemicals can be divided into several categories, described below.

#### Simple *phenols* and *phenolic acids* (C<sub>6</sub>H<sub>5</sub>OH)



**Figure 1: Structures of simple phenol (A) and polyphenols (B)**

*Phenols*, sometimes called *phenolics*, are a class of chemical compounds consisting of a hydroxyl functional group (-OH) attached to an aromatic hydrocarbon group. The simplest of the class is *phenol* ( $C_6H_5OH$ ). Some *phenols* are germicidal and are used in formulating disinfectants. *Phenol*, the parent compound, is used as a disinfectant and for chemical synthesis. *Propolis*, a phenol, is one of the few natural remedies that have maintained its popularity over a long period of time. The pharmacologically active molecules in the *propolis* are *flavonoids* and *phenolic acids* and their esters. These components have multiple effects on bacteria, fungi and viruses. In addition, *propolis* and its components have anti-inflammatory and immunomodulatory activities. Moreover, *propolis* has been shown to lower blood pressure and cholesterol levels. However, clinical studies are required to substantiate these claims. Coffee is particularly rich in bound *phenolic acids*, such as *caffeic acid*, *ferulic acid*, and *P-coumaric acid* [9]. Other substances found to possess *phenolic acids* are *Quince* and *Aloe Ferox*.

Spices are known to significantly contribute to the flavour, taste, and medicinal properties of food due to the presence of *phenolics*. The *phenolic acid* such as *tannic*, *gallic*, *caffeic*, *cinnamic*, *chlorogenic*, *ferulic* and *vanillic acids* is contributory to the flavour of spices. A high amount of *tannic* and *gallic acids* are found in black mustard and clove. *Caffeic*, *chlorogenic* and *ferulic acids* are found in high concentrations in *cumin*. Both *Vanillic*

and *cinnamic acids* are found in onion seeds (*Nigella sativa*).

*Salicylic acid* is a *phenolic* compound which is a precursor compound to aspirin [10]. Amongst the most commonly used *salicylate*, *Aspirin* (*acetylsalicylic acid*) is still the most popularly utilised, as an aqueous solution. Taken orally, aspirin is rapidly absorbed at a low pH within the lining of the stomach. Less rapid absorption is observed with other formulations and this because of the rate limiting step of tablet disintegration. It has been stipulated that the latter factor is due to maximal alkaline in pH. Therefore, the rate of aspirin absorption is dependent on both the formulation and on the rate of gastric emptying. Aspirin absorption follows first-order kinetics with an absorption half-life ranging from five to sixteen minutes. Hydrolysis of aspirin to *salicylic acid* by nonspecific esterases occurs in the liver and, to a lesser extent, the stomach so that only sixty eight percent of the dose reaches the systemic circulation as aspirin. Both aspirin and *salicylic acid* are bound to serum albumin (aspirin being capable of irreversibly acetylating many proteins), and both are distributed in the synovial cavity, central nervous system, and saliva. The serum half-life of aspirin is approximately 20 minutes. The fall in aspirin concentration is associated with a rapid rise in *salicylic acid* concentration. *Salicylic acid* is excreted by the renal system in part unchanged and the rate of elimination is influenced by urinary pH, the presence of organic acids, and the urinary flow rate.

### Benefit of phenols

*Phenolic acids* are plant metabolites widely spread throughout the plant kingdom. *Phenolic* compounds are essential for the growth and reproduction of plants, and are produced as a response for defending injured plants against pathogens. Recent interest in *phenolic acids* stems from their potential protective role, through ingestion of fruits and vegetables, against oxidative damage diseases (coronary heart disease, stroke, and cancers).

The absorption and bioavailability of *phenolics* in humans are controversial. Data on these aspects of *phenolics* are scarce and merely highlight the need for extensive investigations of the handling of *phenolics* by the gastrointestinal tract and their subsequent absorption and metabolism. Plant *phenolic* compounds are diverse in structure and are characterised by hydroxylated aromatic rings (e.g. *flavan-3-ols*). Categorised as secondary metabolites, their function in plants is often poorly understood. Many plant *phenolic* compounds are polymerised into larger molecules such as the *proanthocyanidins* and *lignins*. Furthermore, *phenolic acids* may occur in food plants as esters or glycosides conjugated with other natural compounds such as *flavonoids*, *alcohols*, *hydroxyl fatty acids*, *sterols*, and *glucosides*.

Some herbs such as *tarragon* and *thyme* both contain *caffeic acid*, which is effective against bacteria, viruses and fungi [6]. Both, *catechol* and *pyrogallol* are hydroxylated *phenols*, shown to be toxic against microorganisms [6]. Some authors have found that more highly oxidized *phenols* ascribed biologically active polyphenol components with greater inhibitory effects [11], which possess powerful antioxidant activities. The mechanisms thought to be responsible for *phenolic* toxicity to micro-organisms include enzyme inhibition by the oxidized compounds, possibly through reaction with sulphydryl groups or through more non-specific interactions with the proteins [12]. *Phenolic* compounds possessing a C<sub>3</sub> side chain at a lower level of oxidation are classified as essential oils and often cited as having powerful antioxidant activities [13].

### TERPENOIDS AND ESSENTIAL OILS

Essential oils are plant fragrances, which are enlisted as secondary metabolites. The two primary constituents of essential oils are highly enriched unsaturated

hydrocarbons and oxygenated molecules, with their structure based on the isoprene unit [6]. These organic compounds can further be classified as terpenes, alcohols, esters, aldehydes, ketones and phenols.

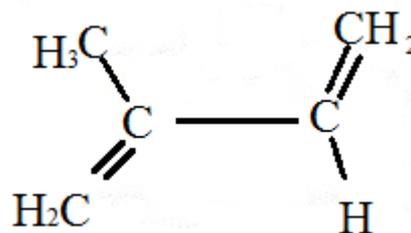


Figure 2: Basic structure of an Isoprene unit

The general chemical formulae of *terpenes* is C<sub>10</sub>H<sub>8</sub>. When the compounds carry an additional element, usually oxygen, these generate *terpenoids*. *Terpenoids* are biosynthesised from acetate units and as such share their origin with fatty acids [6]. However the distinguishing characteristic, from fatty acids, is an extensive branching when cyclized. Some examples of common *terpenoids* include methanol and *Camphor* (*monoterpenes*), *farnesol* and *Artemisinin* (*sesquiterpenoids*) [6]. *Terpenoids* are reported to be active against bacteria [14, 15]. In 1977, it was reported that 60 percent of essential oil derivatives examined to date were inhibitory to fungi while 30 percent inhibited bacteria [16, 17]. It has been speculated that the mode of action of the *terpenes* revolves around the membrane disruption by the lipophilic compounds [6, 18]. Food scientists have found the *terpenoids* present in essential oils of plants to be useful in the control of bacterial growth [19, 20]. *Terpenes* a class of hydrocarbons usually act as building blocks used in many essential oils and fragrances.

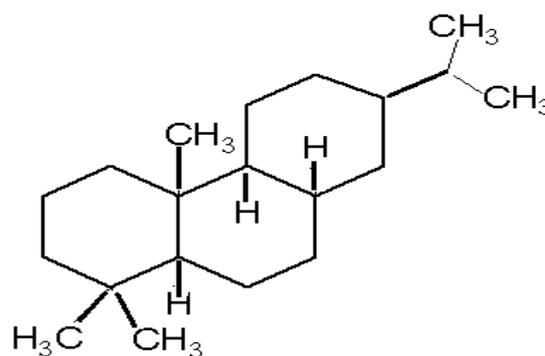


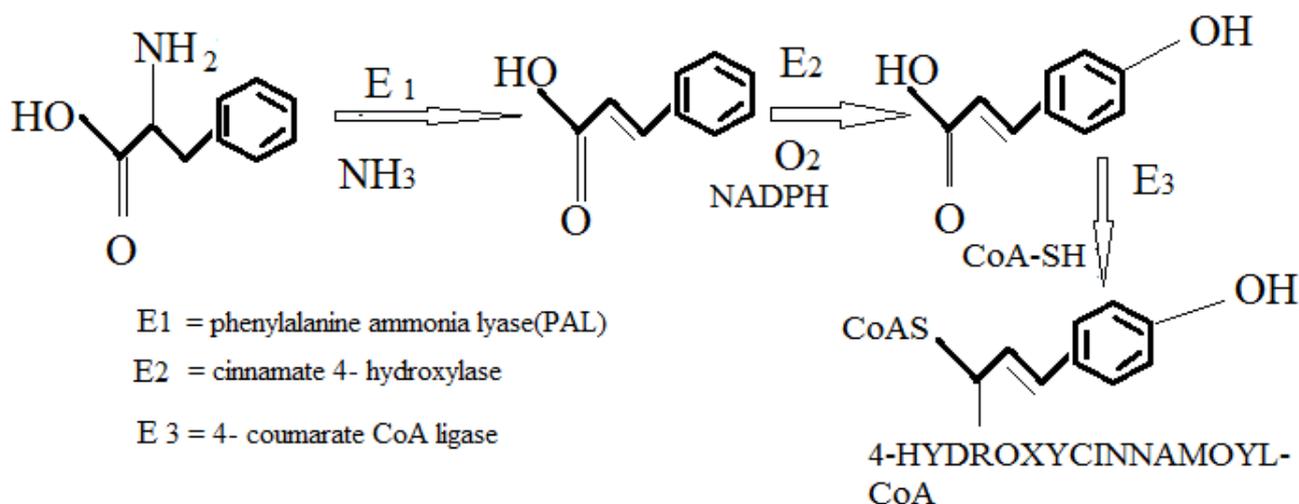
Figure 3: Basic structure of terpenes

**FLAVONES, FLAVONOIDS AND FLAVONOLS**

*Flavones* are *phenolic* structures that containing one carbonyl group and with the addition of a 3-hydroxyl group, the structure yields a *flavonol*. When the compound occur as a C<sub>6</sub>-C<sub>3</sub> unit linked to an aromatic ring, we have *Flavonoids*, a hydroxylated *phenolic* group [6]. As a group of polyphenolic compounds synthesised by the phenyl propanoid pathway, these have been known to respond to various pharmacological and biological actions including anti-inflammatory, antimicrobial and anticancer activity [21, 22,23]. These extensive biological properties extend to antioxidants, in numerous conditions thereby, reducing the risk of diseases [24]. *Catechins*, as a part of the chemical family of flavonoids, possesses two benzene rings, designated A and B and a C ring designated as dihydropyran-heterocycle with a hydroxyl group on carbon3. The most reduced form of the C<sub>3</sub> unit of flavonoid compound, are two isomers, found mostly

as cacao and tea constituents [25]. These isomers share similar properties when they have the same functional group. Catechin and epicatechin are the building blocks of the proanthocyanidins, a type of condensed tannin. As an immunomodulatory it oxidises using catechol radical oxidation as a defence mechanism against plant pathogens [26, 27].

*Catechin* easily binds to proteins, blocking bacteria from adhering to cell walls thereby, disrupting their ability to cause destruction [28]. It decreases cholesterol level in blood and prevents LDL cholesterol caused by oxidation. This mechanism prevents narrowing of blood vessels caused by the build-up of LDL cholesterol. *Catechin* is a useful component for the prevention and treatment of substances that suppresses the immune system by preventing influenza against bacteria and viruses [29].



**Figure 4: Biosynthesis of *Catechins***

*Flavone* is one of the main groups of *flavonoids*, and the most widespread *flavone* is *quercetin* which serves as the backbone for other *flavonoids*. Many medicinal plants have significant *quercetin* content. *Quercetin* behaves like auxins in stimulating the germination of wheat seeds. The possible function of the colouring matter present in the compound may be in insect-pollinated flowers and edible

fruits. The type of diversity make both flowers and fruit more conspicuous so that seed dispersion is aided by animals [30]. It has been noticed that small quantities of *quercetin* may act as cardiac stimulants to strengthen weak capillary blood vessels [30].

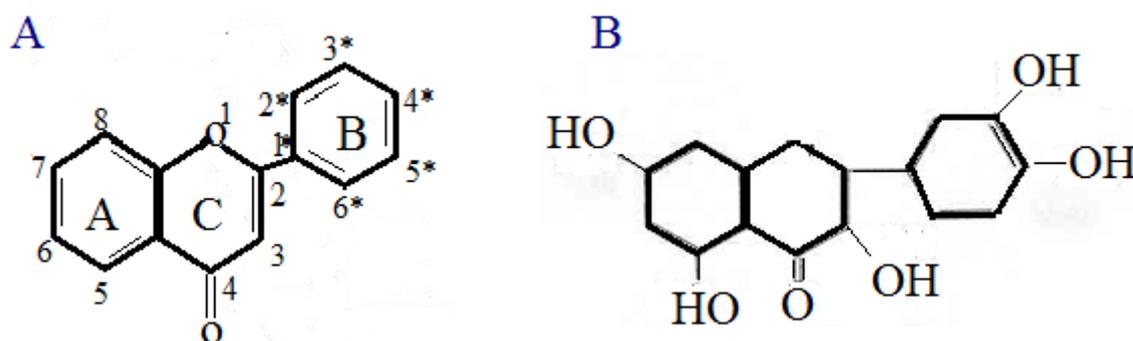


Figure 5: Structure of *Flavonoid* (A) and *Quercetin* (B)

### Tannins

*Tannins* by definition have the ability to react with protein, forming stable water insoluble co-polymers [8]. The compound is of plant origin, which through their ability to cross-link with protein, are capable of transforming raw animal skin into leather. Plant tissues high in tannin content impart an astringent taste, which acts as a deterrent to most feeders. Divided into two groups, according to the chemical structure and properties, tannins could be hydrolysable tannins (HT) or condensed tannins (CT) [31].

Hydrolysable *tannins* are based on *gallic acid*, usually as multiple esters with D-glucose while the condensed *tannins* are derived from flavonoid monomers [6; 32]). *Tannins* may be formed by polymerisation of quinone units. Many human physiological activities, such as stimulation of phagocytic cells, host mediated tumour activity and a wide range of anti-infective actions have been assigned to *tannins* [33]. Their mode of antibacterial action is related to their ability to inactivate microbial adhesions, enzymes and cell envelope transport proteins. Evidence supports direct inactivation of micro-organisms. [6, 33]

### QUINONES

*Quinones* contain aromatic rings [6]. The compounds are ubiquitous in nature and are characteristically highly reactive. Although are widely distributed with great structural variation, *quinones* make relatively little contribution to colour in higher plants [8]. Commonly present in bark, roots, or else in tissues (such as leaves) their colours are masked by other pigments. These compounds, are responsible for the browning reaction in cut or injured fruits and vegetables. As an intermediate in the melanin synthesis pathway of the human skin,

*quinones* provide a source of stable free radicals. Known to complex irreversibly with *nucleophilic amino acids* in proteins, the compound, often leads to inactivation of protein and loss of function [34]. For this reason, the potential range of *quinone* antimicrobial effect is increased targeting microbial cell surface-exposed adhesions, cell wall polypeptides, and membrane-bound enzymes [6]. *Quinones* may also render substrates unavailable to the microorganisms. One example of a *quinone* is *p-benzoquinone* and the basic chemical structure is given in Figure 6.



Figure 6: Basic structure of *p-benzoquinone*

Indiscriminate use of antibiotics and prescriptions has been linked together as one of the instrumental factors leading to the emergence of multidrug resistant organisms (MDROs) in the community/hospital [35, 36]. Unabated spread and proliferation of AMR genes among pathogenic bacteria has regrettably been the cause of high morbidity and mortality among critically ill patients, and has been found to contribute substantially to rising cost of healthcare due to prolong admission and expensive drugs for treatments annually [37,38]. *Pseudomonas aeruginosa* is a Gram-negative, rod shaped; motile

bacterium found abundant in various habitats and has been implicated in several human infections. Most *P. aeruginosa* infections are difficult to treat due to its ability to resist many structurally unrelated antibiotics, which is because of the presence of intrinsic and acquired antibiotic resistance mechanisms [39]. Antimicrobial drug resistance mechanisms and its acquisition in *P. aeruginosa* are remarkable, to the favour of the pathogen. Several mechanisms of resistance to antimicrobial agents ranging from efflux pump to mobile genetic elements and hydrolysing enzymes have been described in clinical isolates of *P. aeruginosa* [40, 41]. Notably among these mechanisms is the production of various classes of  $\beta$ -lactamases that mediates their resistance to beta-lactam drugs. Over the last decades, enzymes in this category have been detected in *P. aeruginosa*, especially extended-spectrum beta-lactamase (ESBL) such as OXA, VEB, PER, SHV and TEM types of ESBL [41, 42].

#### Conflict of Interests

The authors declare that they do not have any conflict of interests.

#### Acknowledgement

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