

## Pharmacognosy and Medicinal Chemistry of Traditional Chinese Medicine

Sandhya Jinesh<sup>1</sup> and Rajan Radhakrishnan<sup>2</sup>

<sup>1</sup>West Haven Pharmacy, West Haven CT, USA,

<sup>2</sup>Mohammed Bin Rashid University College of Medicine, Dubai, UAE

\***Corresponding Author:** Sandhya Jinesh, West Haven Pharmacy West Haven, CT 06516 Tel: +1-845-893-2716 E-mail: smenon.rx@gmail.com

**Received Date:** October 10, 2022 **Accepted Date:** November 10, 2022 **Published Date:** November 13, 2022

**Citation:** Jinesh Sandhya, Rajan Radhakrishnan(2022) Pharmacognosy and Medicinal Chemistry of Traditional Chinese Medicine. J Med Plant Herbs 1: 1-13.

### Abstract

Traditional Chinese Medicine (TCM) is an ancient system of medicine that is based on a holistic approach to the human body. One of the major problems facing TCM, as with other traditional medical systems, is the difficulty with authentication of the drugs and quality control of its formulations. Majority of the drugs used in TCM are derived from plants. Therefore, in the current review, we researched pharmacognostic methods that are used to standardize and authenticate TCM drugs. We found that, with the advance of science and technology, several physicochemical methods are being utilized to standardize TCM drugs. Modern pharmacognosy is very much dependent on phytochemical techniques. We have summarized the common pharmacognostic and chemical analytical methods used to authenticate TCM drugs and to correlate the TCM properties of these drugs to their chemical nature. Chemical analytic techniques are extremely valuable in authentication and quality control of plant-based drugs and their formulations found in traditional systems such as TCM, Ayurveda, and Kampo.

**Keywords:** Traditional Chinese Medicine; TCM; Pharmacognosy; Phytochemistry; Chemical Analysis; Quality Control; Medicinal Chemistry

## Introduction

Traditional Chinese Medicine (TCM) is an ancient system of medicine which is based on holistic treatment of the human body in health and disease. In TCM, the balance and harmony between several physical and spiritual components of the human body are of utmost importance--for example the balance between Ying and Yang and relationship of 5 elements to different organs etc [1]. A physician or scientist trained purely in modern science may not be able to fully appreciate and understand these theories of balance and harmony that cannot be explained based on our current knowledge of science. One of the current major problems with TCM is the absence of evidence of clinical efficacy from randomized controlled

clinical studies [2]. Also, the quality control and authentication process of TCM medications pose great challenges. The vast majority of the drugs used in TCM are of plant origin (Table 1), although some animal tissues are also in TCM. Several laboratories have sought to study the physio- chemical nature and pharmacological effects of TCM medications using modern techniques. A major characteristic of TCM formulations is the complexity of the ingredients [3]. This creates a major problem with maintaining consistency between different practitioners or manufacturers who formulate TCM medications, and also hinders quality control and clinical efficacy studies. These problems exist with medications in other ancient systems of medicines, including Ayurveda, Unani, Kampo etc.

| Drug                             | Clinical use                           | Traditional use                  | Plant name                                      | Common name       | TCM name |
|----------------------------------|--|----------------------------------|---|-------------------|----------|
| Aescin                           | anti-inflammatory                      | anti-inflammatory                | <i>Aesculus hippocastanum</i>                   | horse chestnut    | 炒櫛子      |
| Aesculetin                       | anti-dysentery                         | anti-dysentery                   | <i>Fraxinus rhychophylla</i><br><i>Hance</i>    | ash bark          | 白蠟樹皮     |
| Agrimophol                       | anthelmintic                           | anthelmintic                     | <i>Agrimonia pilosa</i>                         | agrimony          | 仙鶴草      |
| Ajmalicine                       | anti-arrhythmia                        | tranquillizer                    | <i>Rauwolfia serpentina</i>                     | Indian snake root | 蘿芙木      |
| Artesunate                       | anti-malarial                          | treatment of fever, chills       | <i>Artemisia annua</i>                          | sweet wormwood    | 青蒿       |
| Deserpidine                      | anti-hypertensive                      | anti-hypertensive                | <i>Rauwolfia serpentina</i>                     | Indian snake root | 蘿芙木      |
| Allyl isothiocyanate             | rubefacient                            | rubefacient                      | <i>Brassica alba</i>                            | mustard           | 芥子       |
| Andrographolide                  | anti-dysentery                         | anti-dysentery                   | <i>Andrographis paniculata</i><br><i>Ness</i>   | andrographis herb | 穿心蓮      |
| Arecoline                        | anthelmintic                           | anthelmintic                     | <i>Areca catechu</i> L.                         | betel nut         | 檳榔       |
| Asiaticoside                     | vulnerary                              | vulnerary                        | <i>Centella asiatica</i> L. Urban               | centella          | 積雪草, 崩大碗 |
| Atropine                         | anti-cholinergic                       | pupil dilation                   | <i>Atropa belladonna</i> Linné                  | deadly nightshade | 茄蔴       |
| Berberine                        | anti-dysentery                         | treatment of gastric ailments    | <i>Berberis sargentiana</i>                     | Chinese barberry  | 刺黃蓮      |
| Caffeine                         | stimulant                              | stimulant                        | <i>Camellia sinensis</i> (L)<br><i>Kuntze</i>   | tea               | 茶        |
| (+)-Catechin                     | haemostatic                            | haemostatic                      | <i>Potentilla fragarioides</i> L.               | dewberry          | 委陵菜      |
| Cocaine                          | local anaesthetic                      | stimulant                        | <i>Erythroxylum coca</i> Lamk                   | coca              | 古柯       |
| Codeine, morphine and papaverine | analgesic                              | analgesic                        | <i>Papaver somniferum</i> L.                    | opium             | 罌粟       |
| Colchicines and demecolone       | anti-tumour                            | anti-gout                        | <i>Colchicum autumnale</i> L.                   | colchicum seed    | 秋水仙      |
| Curcumin                         | choleric                               | choleric                         | <i>Curcuma longa</i> L.                         | ginger            | 薑黃       |
| Sennoside                        | laxative                               | laxative                         | <i>Cassia acutifolia</i> Delile                 | senna             | 尖葉番瀉樹    |
| Digoxin and deslanoside          | cardiotonic                            | cardiotonic                      | <i>Digitalis lanata</i>                         | foxglove          | 長葉毛地黃    |
| Digitoxin and gitalin            | cardiotonic                            | cardiotonic                      | <i>Digitalis purpurea</i>                       | foxglove          | 毛地黃      |
| Emetine                          | amoebicide, emetic                     | amoebicide, emetic               | <i>Cephaelis ipecacuanha</i>                    | ipecac            | 吐根       |
| Ephedrine and norepinephrine     | sympathomimetic                        | chronic bronchitis               | <i>Ephedra sinica</i> Stapf                     | ma huang root     | 麻黃       |
| Hyoscyamine                      | anti-cholinergic                       | sedative                         | <i>Hyoscyamus niger</i> L.                      | henbane           | 莨菪       |
| Kainic acid                      | ascaricide                             | anthelmintic                     | <i>Digenea simplex</i>                          | digenea           | 鱒鴿菜      |
| α-Lobeline                       | smoke deterrent, respiratory stimulant | expectorant                      | <i>Lobelia inflata</i> L.                       | Chinese lobelia   | 半邊蓮      |
| Quinidine                        | anti-arrhythmic                        | anti-malarial                    | <i>Cinchona officinalis</i>                     | cinchona bark     | 金雞納      |
| Quinine                          | anti-malarial                          | anti-malarial                    | <i>Cinchona officinalis</i>                     | cinchona bark     | 金雞納      |
| Quisqualic acid                  | anti-helminthic                        | antihelminthic                   | <i>Quisqualis indica</i> L.                     | rangoon creeper   | 使君子      |
| Rhomitoxin                       | anti-hypertensive, tranquillizer       | anti-hypertensive                | <i>Rhododendron molle</i> G. Don                | yellow azalea     | 鬧羊花      |
| Rotundine, tetrandrine           | anti-hypertensive                      | anti-hypertensive                | <i>Stephania tetrandra</i> S. Moore             | fangchi           | 漢防己      |
| Salicin                          | analgesic                              | analgesic                        | <i>Salix alba</i> L.                            | willow            | 柳        |
| Scopolamine                      | sedative                               | sedative                         | <i>Datura metel</i> L.                          | thorn apple leave | 曼陀羅      |
| Silymarin                        | anti-hepatotoxic                       | treatment of liver disorders     | <i>Silybum marianum</i> (L)<br><i>Gaertn</i>    | holy thistle      | 水飛薊      |
| Strychnine                       | stimulant                              | stimulant                        | <i>Strychnos nux-vomica</i> L.                  | nux vomica        | 馬錢子      |
| Tetrahydrocannabinol             | anti-emetic, reduces ocular tension    | treatment of intestinal problems | <i>Cannabis sativa</i> L.                       | hemp              | 大麻       |
| Tetrahydropalmatine              | analgesic, sedative, tranquillizer     | sedative                         | <i>Corydalis ambigua</i> (Pallas) Cham. et Schi | corydalis         | 延胡索      |
| Theobromine, theophylline        | diuretic, vasodilator                  | diuretic                         | <i>Camellia sinensis</i> (L)<br><i>Kuntze</i>   | tea               | 茶        |

**Table1:** Comparison of TCM use and modern clinical use of some of the herbal medicines.

(Source: Efferth et al., 2007)

Despite these many problems, there has been a recent upsurge of interest in ancient traditional medical systems in the West, mostly because several anticancer compounds were isolated from natural medicinal products used by traditional systems of medicine. There is still a need for newer anticancer agents since only a limited proportion of cancer patients respond favorably to commonly prescribed chemotherapeutic drugs. The majority of anticancer agents in current clinic use are either naturally occurring or derivatives of natural products, such as *Vinca* alkaloids, taxanes, podophyllotoxin, camptothecins and anthracyclines. Hundreds of scientific papers have studied the anti-cancer properties of natural products including those used in TCM. Efforts have been undertaken by several scientists who are knowledgeable both in TCM and modern science/medicine to identify the individual pharmacological activities of the components in TCM formulations. Usually, scientists are unable to relate the pharmacological or clinical effects of TCM to one ingredient or chemical constituent present in the TCM formulation. As in other traditional system remedies it is hypothesized that the various ingredients in TCM act synergistically to produce the intended clinical effect. It is also thought that some of the ingredients in these formulations act to reduce the adverse effects of some of the other active ingredients. Chinese University of Hong Kong is one of the prominent institutions trying to scientifically study TCM drugs and they publish a journal named *Abstracts of Chinese Medicine* that publishes English abstracts of TCM studies published in other languages. One of the difficulties in testing the quality of TCM products is the lack of consistency in the identity of the components used in TCM such as plant products, animal products and minerals. Since herbs form the major constituents of TCM formulations, pharmacognosy and medicinal chemistry of natural products is of utmost importance to studying TCM scientifically and to assessing the quality and authenticity of TCM products.

## Pharmacognosy and Medicinal Chemistry of TCM

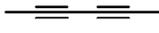
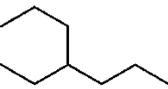
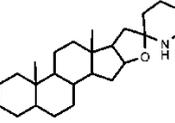
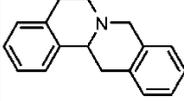
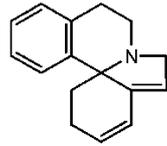
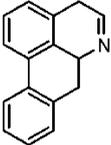
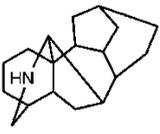
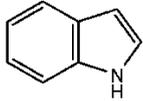
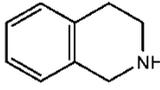
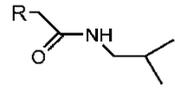
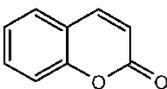
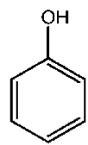
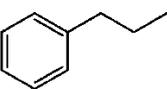
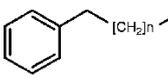
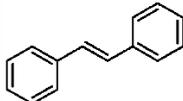
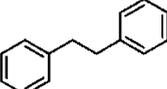
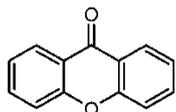
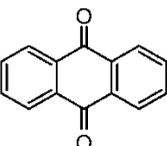
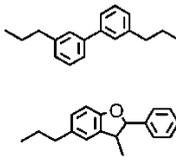
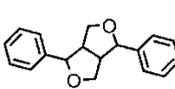
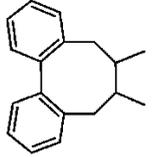
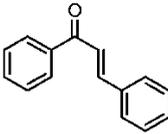
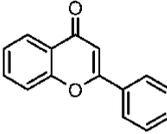
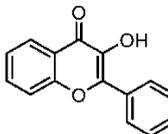
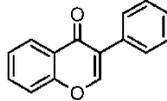
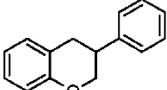
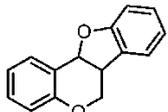
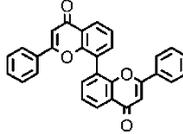
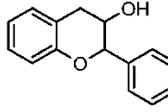
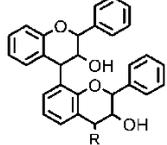
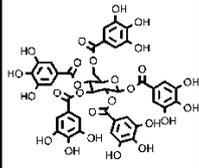
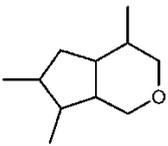
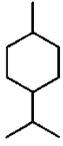
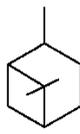
Pharmacognosy is the study of medicinal substances derived from natural sources. The constituents of TCM formulations are derived from natural sources. Since these substances do not exist in the form of pure chemicals as in the case of modern drugs, identification and authentication pose a big challenge to scientists who try to study TCM using modern scientific methods. The problem is complicated by the complexity of the constituents present in single TCM formulations. This is where pharmacognosy and medicinal chemistry can contribute to scientific studies of TCM. In pharmacognosy, drugs are identified by their botanical characteristics, microscopic properties and chemical characteristics. Pharmacognosy utilizes several techniques in phytochemistry to characterize the drugs chemically and to isolate and identify the possible active compounds in the natural products. WHO monographs of natural products typically includes the following pharmacognostic details: definition, synonyms, vernacular names, geographical distribution, description of the plant/source, general appearance of the crude drug material, organoleptic properties, microscopic characteristics, powdered material description, general identity tests, purity tests, chemical assays, major chemical constituents and medicinal uses [4]. The original techniques used in pharmacognosy to identify drugs were based on the morphology and organoleptic characteristics. With the advancement of science and technology, other methods such as microscopy and physicochemical testing methods are being utilized in pharmacognostic studies. Among these, phytochemistry plays an important role in identifying herbal drugs used in traditional medicine systems. Most of the pharmacologically active compounds in plants are secondary metabolites. Major active chemical compounds present in medicinal herbs used in TCM are of the following nature: aliphatics, alkaloids, simple phenolics, lignans, quinones, polyphenols (flavonoids and tannins), and mono-, sesqui-, di-, and triterpenes (Table 2, Table 3) [5], have done a very systematic study of phytochemicals in TCM and their possible relationships with the TCM properties (Table 2 and 3).

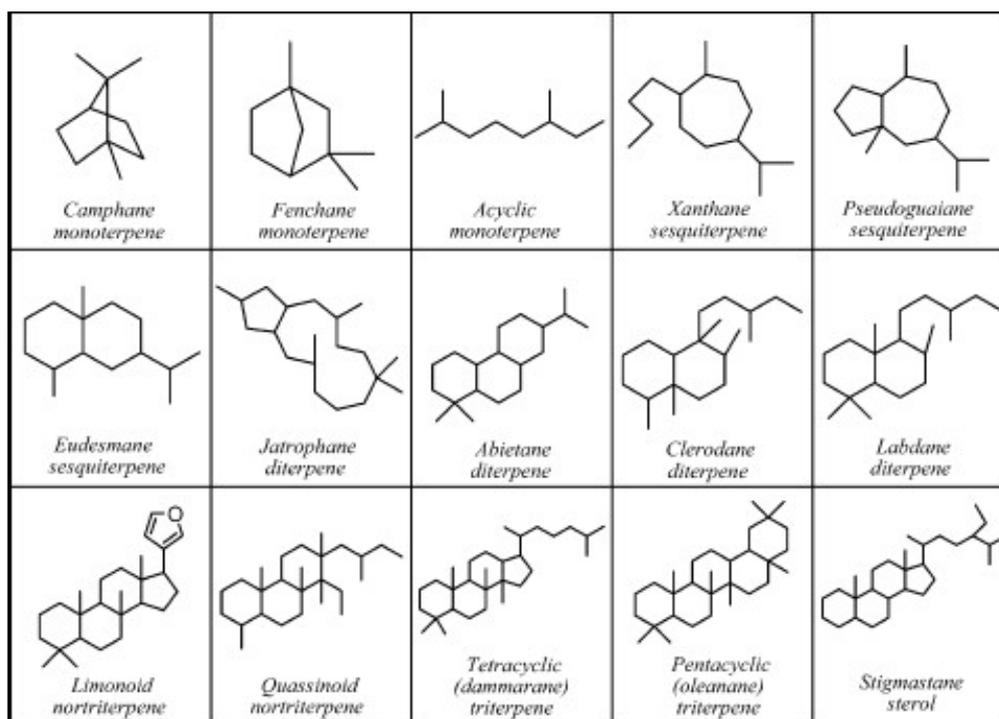
**Table 4.** Descriptions of SOM-Ward Clusters<sup>a</sup>

| phytochemical class(es)                              | CN | NC  | TCM profile   | skeletal type   | glycosides (%) | MW (mean) | log P (mean) |
|--|----|-----|---|---|----------------|-----------|--------------|
| aliphatic  | 16 | 64  | <i>Tonify Qi, Stop Bleeding, Tonify Blood, Wind Heat</i>                        | acetylene   | 0              | 286       | 5.30         |
| aliphatic, simple phenolic                           | 36 | 589 | <i>Wind Cold, Invigorate Blood, Drain Dampness</i>                              | low MW, volatile  | 5              | 250       | 3.47         |
| alkaloid   | 27 | 263 | <i>Emetic, Phlegm Heat</i>  | steroidal   | 14             | 475       | 3.40         |
|  | 29 | 186 | <i>Astringent, Damp Heat, Cough &amp; Wheezing, Drain Dampness</i>              | protoberberine, erythrina, aporphine  | 4              | 345       | 2.82         |
|  | 31 | 226 | <i>Astringent, Internal Wind, Cough &amp; Wheezing, Phlegm Cold, Toxic Heat</i> | mixed   | 10             | 355       | 1.87         |
| alkaloid, <sup>1</sup> simple phenolic               | 37 | 591 | <i>Internal Cold, Stop Bleeding, Astringent</i>                                 | diterpene, <sup>1</sup> indole, <sup>1</sup> isoquinoline, <sup>1</sup> isobutylamide <sup>1</sup>              | 12             | 427       | 2.77         |
| simple phenolic, <sup>1</sup> diterpene <sup>2</sup> | 18 | 166 | <i>Phlegm Heat, Wind Damp</i>   | coumarin, <sup>1</sup> jatrophone, <sup>2</sup> abietane <sup>2</sup>   | 6              | 487       | 3.94         |
| simple phenolic                                      | 28 | 273 | <i>Wind Cold, Internal Cold, Phlegm Cold</i>                                    | phenol, phenylpropanoid, long-chain aromatic  | 2              | 234       | 2.44         |
|  | 33 | 426 | <i>Laxative, Tonify Yang, Heat (Blood)</i>                                      | stilbene, xanthone, phenylpropanoid, phenol   | 66             | 415       | 0.05         |
|  | 38 | 651 | <i>Aromatic (Damp), Invigorate Blood, Regulate Qi</i>                           | coumarin, long-chain aromatic, phenylpropanoid, phenol, dibenzyl  | 6              | 287       | 2.78         |
| lignan   | 6  | 31  | <i>Wind Cold, Internal Cold, Astringent</i>                                     | neolignan, furo- and epoxy-tetrahydrofuranoid   | 0              | 371       | 3.15         |
|  | 10 | 44  | <i>Tonify Yang, Wind Damp</i>   | neolignan, furofuranoid   | 87             | 561       | 0.29         |
|  | 12 | 45  | <i>Astringent</i>   | dibenzocyclooctadiene   | 0              | 434       | 4.10         |
| quinone  | 8  | 70  | <i>Laxative, Tonify Yang, Stop Bleeding</i>                                     | anthraquinone   | 16             | 304       | 2.13         |
| polyphenol   | 1  | 11  | <i>Cough &amp; Wheezing, Tonify Yin</i>   | flavonol  | 0              | 299       | 2.30         |
|  | 20 | 91  | <i>Astringent, Stop Bleeding</i>  | tannin, biflavonoid   | 27             | 753       | 2.71         |
|  | 23 | 157 | <i>Wind Heat, Tonify Blood, Damp Heat</i>                                       | flavonoid, isoflavonoid, chalcone   | 55             | 478       | 0.82         |
|  | 35 | 480 | <i>Damp Heat, Tonify Qi, Tonify Yang</i>  | flavonoid, isoflavonoid, chalcone   | 25             | 400       | 2.44         |
|  | 40 | 831 | <i>Toxic Heat, Tonify Yang, Tonify Yin, Cough &amp; Wheezing</i>                | flavone, flavonol   | 46             | 496       | 1.29         |
| polyphenol, <sup>1</sup> lignan <sup>2</sup>         | 21 | 105 | <i>Damp Heat, Tonify Yang</i>   | isoflavonoid, <sup>1</sup> pterocarpan, <sup>1</sup> neolignan <sup>2</sup>                                     | 21             | 392       | 2.40         |
| polyphenol, <sup>1</sup> quinone <sup>2</sup>        | 24 | 167 | <i>Laxative, Astringent</i>   | flavan-3-ol, <sup>1</sup> gallate ester, <sup>1</sup> proanthocyanidin, <sup>1</sup> anthraquinone <sup>2</sup> | 61             | 555       | 1.32         |
| monoterpene  | 25 | 130 | <i>Heat (Blood), Tonify Yang, Heat (Qi)</i>                                     | iridoid, menthane, pinane   | 60             | 348       | -1.04        |
|  | 32 | 403 | <i>Internal Cold, Wind Cold, Phlegm (Heart)</i>                                 | menthane, thujane, camphane, pinane, fenchane, acyclic  | 0              | 148       | 2.97         |
| sesquiterpene  | 15 | 63  | <i>Phlegm Cold, Wind Damp</i>   | lactones, xanthane, pseudoguaiane, eudesmane  | 0              | 326       | 1.47         |
|  | 39 | 613 | <i>Regulate Qi, Invigorate Blood, Aromatic (Damp)</i>                           | many types  | 0              | 232       | 3.49         |
| diterpene, <sup>1</sup> nortriterpene <sup>2</sup>   | 17 | 75  | <i>Cathartic, Toxic Heat, Astringent</i>  | tricyclic, <sup>1</sup> quassinoid <sup>2</sup>   | 15             | 427       | 0.21         |
| diterpene, <sup>1</sup> triterpene <sup>2</sup>      | 30 | 229 | <i>Invigorate Blood, Wind Damp, Phlegm Heat</i>                                 | abietane, <sup>1</sup> clerodane, <sup>1</sup> labdane, <sup>1</sup> dammarane <sup>2</sup>                     | 2              | 340       | 3.08         |
| triterpene   | 2  | 11  | <i>Damp Heat, Toxic Heat</i>  | quassinoid  | 0              | 430       | 2.19         |
|  | 3  | 28  | <i>Shen</i>   | tetracyclic   | 3              | 518       | 3.14         |
|  | 4  | 22  | <i>Toxic Heat</i>   | sterol  | 82             | 614       | 0.42         |
|  | 5  | 29  | <i>Tonify Qi</i>  | sterol  | 76             | 643       | 2.06         |
|  | 7  | 23  | <i>Toxic Heat, Invigorate Blood, Tonify Yang</i>                                | pentacyclic   | 0              | 458       | 6.56         |
|  | 9  | 61  | <i>Wind Heat</i>  | pentacyclic   | 54             | 618       | 3.35         |
|  | 11 | 86  | <i>Shen, Drain Dampness</i>   | tetracyclic   | 0              | 543       | 3.43         |
|  | 13 | 60  | <i>Toxic Heat, Wind Heat, Phlegm Cold</i>                                       | pentacyclic   | 56             | 827       | 1.36         |
|  | 14 | 85  | <i>Regulate Qi</i>  | limonoid  | 4              | 588       | 2.81         |
|  | 19 | 130 | <i>Drain Dampness, Shen</i>   | tetracyclic   | 2              | 484       | 4.87         |
|  | 22 | 142 | <i>Tonify Qi, Stop Bleeding, Wind Heat</i>                                      | tetracyclic   | 82             | 723       | 2.01         |
|  | 26 | 193 | <i>Tonify Yin, Tonify Yang, Internal Wind, Heat (Qi)</i>                        | sterol  | 61             | 695       | 2.74         |
|  | 34 | 561 | <i>Drain Dampness, Wind Damp, Wind Heat, Toxic Heat</i>                         | pentacyclic   | 45             | 636       | 3.30         |

**Table 2:** Phytochemical classes of compounds and TCM properties of some herbal medicines.

(Source: Ehrman et al., 2007.)

|   |  |  |   |   |
|---|--|--|---|---|
| <br><i>Acetylene (example)</i>             | <br><i>Low MW aliphatic (example)</i> | <br><i>Steroidal alkaloid</i>       | <br><i>Protoberberine alkaloid</i>              | <br><i>Erythrina alkaloid</i>                  |
| <br><i>Aporphine alkaloid</i>              | <br><i>Diterpene alkaloid</i>         | <br><i>Indole alkaloid</i>          | <br><i>Isoquinoline alkaloid</i>                | <br><i>Isobutylamide (variable chain)</i>      |
| <br><i>Coumarin</i>                        | <br><i>Phenol</i>                     | <br><i>Phenylpropanoid</i>          | <br><i>Long chain aromatic (variable chain)</i> | <br><i>Stilbene</i>                            |
| <br><i>Dibenzyl</i>                       | <br><i>Xanthone</i>                  | <br><i>Anthraquinone</i>           | <br><i>Neolignans (two types)</i>              | <br><i>Furofuranoid lignan</i>                |
| <br><i>Dibenzocyclooctadiene lignan</i>  | <br><i>Chalcone</i>                 | <br><i>Flavone</i>                | <br><i>Flavonol</i>                           | <br><i>Isoflavone</i>                        |
| <br><i>Isoflavan</i>                     | <br><i>Pterocarpan</i>              | <br><i>Biflavonoid</i>            | <br><i>Flavan-3-ol</i>                        | <br><i>Proanthocyanidin (variable units)</i> |
| <br><i>Hydrolyzable tannin (example)</i> | <br><i>Iridoid monoterpene</i>      | <br><i>p-Menthane monoterpene</i> | <br><i>Pinane monoterpene</i>                 | <br><i>Thujane monoterpene</i>               |

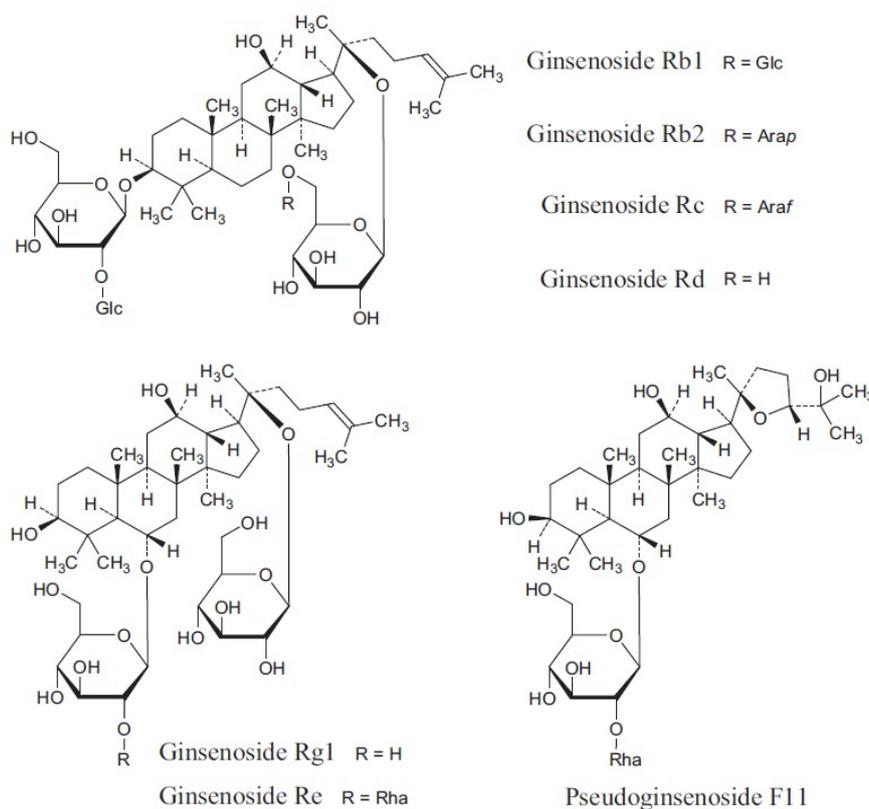


**Table 3:** Types of phytochemical classes seen in TCM drugs

(Source: Ehrman et al., 2007)

One of the most popular examples for the application of pharmacognostic and phytochemical principles in TCM is the identification of the appropriate kind of ginseng used in TCM for various ailments. Ginseng is one of the top selling herbal drugs around the globe, and is used very frequently in TCM and other nutraceutical preparations. Considering its widespread use, both United States Pharmacopoeia (USP) and European Pharmacopoeia (Ph Eur) have included monographs for *Panax ginseng* (Korean or Asian ginseng) and *P. quinquefolius* (American ginseng). Compounds from Ginseng have been shown to have anticancer properties and also increase ubiquitination of multi drug resistant 1 (MDR1) gene that is responsible for the production of P-glycoproteins that pumps out some of the antitumor drugs from the cells [6,7]. Different species of Ginseng are available in the market, although *P. ginseng* (Korean or Asian ginseng) is mainly used in TCM

preparations. One of the major groups of marker compounds used for identification and quality control of Ginseng are ginsenosides. Ginsenosides are triterpenes which are polar in nature (Figure 1). The four common aglycone moieties present in these ginsenosides are protopanaxadiol, protopanaxatriol, ocotillol-type and oleanolic acid. The sugar moiety attached to the aglycones is important in determining their bioactivity. For example, if there are no sugar moieties attached to the 20-position of the aglycone, the ginsenoside acts as a prooxidant (e.g., Rg3, Rh2, and Rg2). If a glucose molecule is attached to the 6-position instead of the 20-position, that makes the ginsenoside an antioxidant (e.g., Rh1) [8]. Different species of Ginseng contain different types of ginsenosides and the content of ginsenosides varies from one species to another. For example, Ginsenoside Rf is Asian ginseng (*P. ginseng*) specific while 24(R)-pseudoginsenoside F11 is specific to American ginseng (*P. quinquefolius*) [9,10].



Chemical structures of ginsenosides

(Sources: WHO monographs on selected medicinal plants. 2009. 4; Yoon et al., 1998).

Testing for the presence or absence of some of these specific compounds is a very reliable chemical method for detecting the authenticity or adulteration of TCM ingredients and formulations. Absolute quantification of chemical constituents can sometimes lead to problems because the content of these secondary metabolites may vary depending on the climate, geographical location and nutrition. A more reliable method is to calculate the ratio between the contents of the marker compounds, which appears to be constant for a given species. Thus Rg1/Re and Rb2/Rc ratios of ginsenosides are constant for *P. ginseng* and *P. quinquefolius* irrespective of their origin, and may be used as a more specific criterion for identification. Thus, determining the ratio between two constituents in a plant drug is more dependable in identifying a plant drug than quantifying single compounds. Thin layer chromatography (TLC) is often used in pharmacognosy and very often used for the authentication of Ginseng. However more sensitive methods such as HPLC and LC-MS techniques are also used in several laboratories to identify these TCM drugs. TLC is a very easy, cost effective and versatile technique for

the fingerprint analysis of plant extracts. United States Pharmacopoeia and European Pharmacopoeia still recommend TLC for the identification of plant-derived drugs [Fuzzati N., 2004]. *P. ginseng* and *P. quinquefolius* can be differentiated using TLC with a mixture of chloroform, methanol and water (13:7:2) as the first developing solvent system (SS-I) and a mixture of water, *n*-butyl alcohol and ethyl acetate (5:4:1) as the second solvent developing system (SS-II). Anisaldehyde reagent is usually used as the spray reagent. This method separates Ginsenosides F11, Rg1, Rg2, Rf, Rc, Rd, Rb2, Rb1 and Ro. Ginsenoside F11 and Rf being specific to *P. ginseng* and *P. quinquefolius* respectively, this method can be used to detect the presence of these two major ginsengs in herbal formulations [Fuzzati N., 2004].

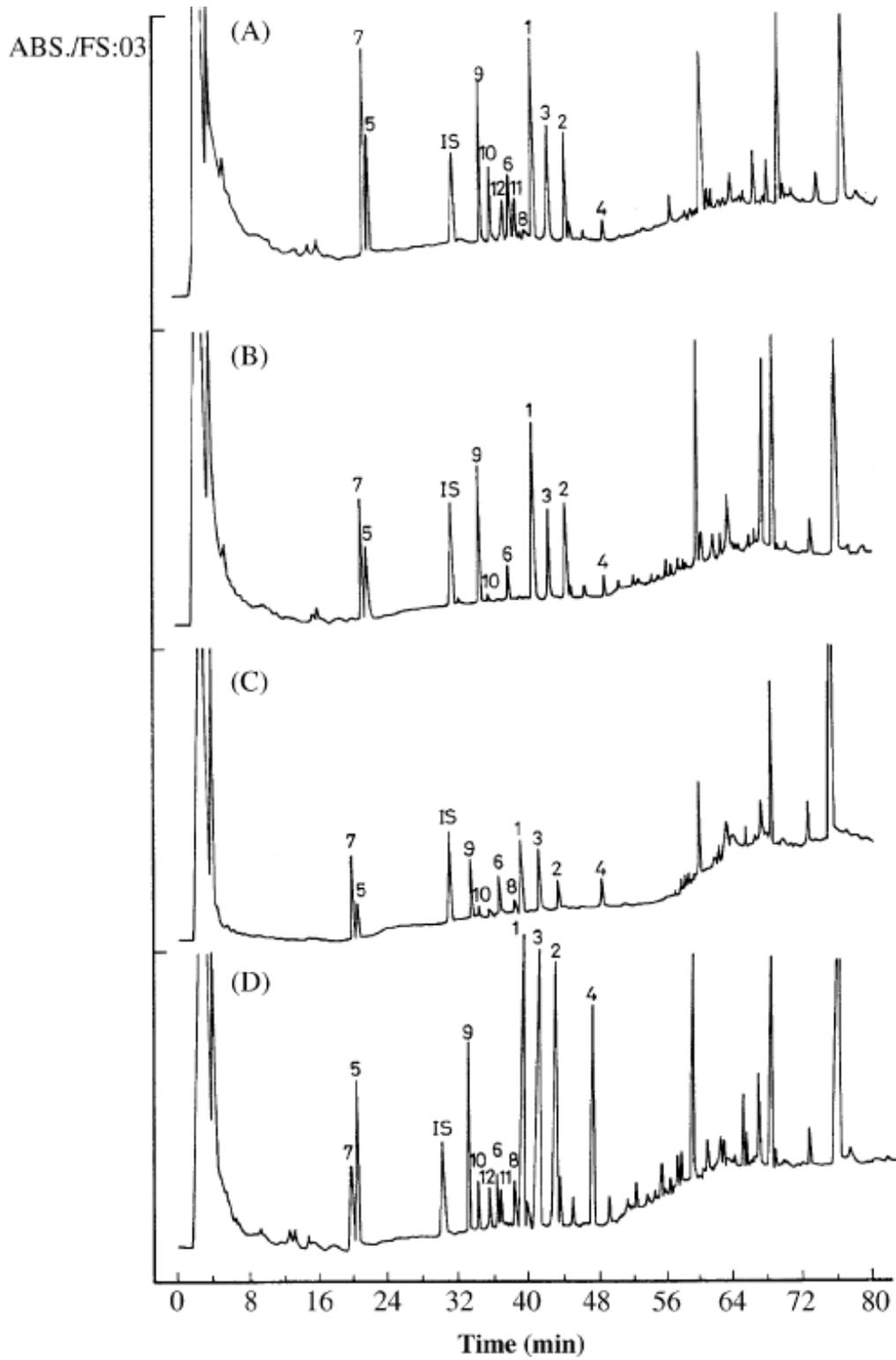
High performance liquid chromatography (HPLC) is another technique that is commonly used to detect the phytochemicals in plant-derived drugs. HPLC provides a fast, sensitive and efficient way to analyze the phytochemicals. It is ideal for analyzing Ginsenosides which are polar saponins. HPLC also has the advantage of using

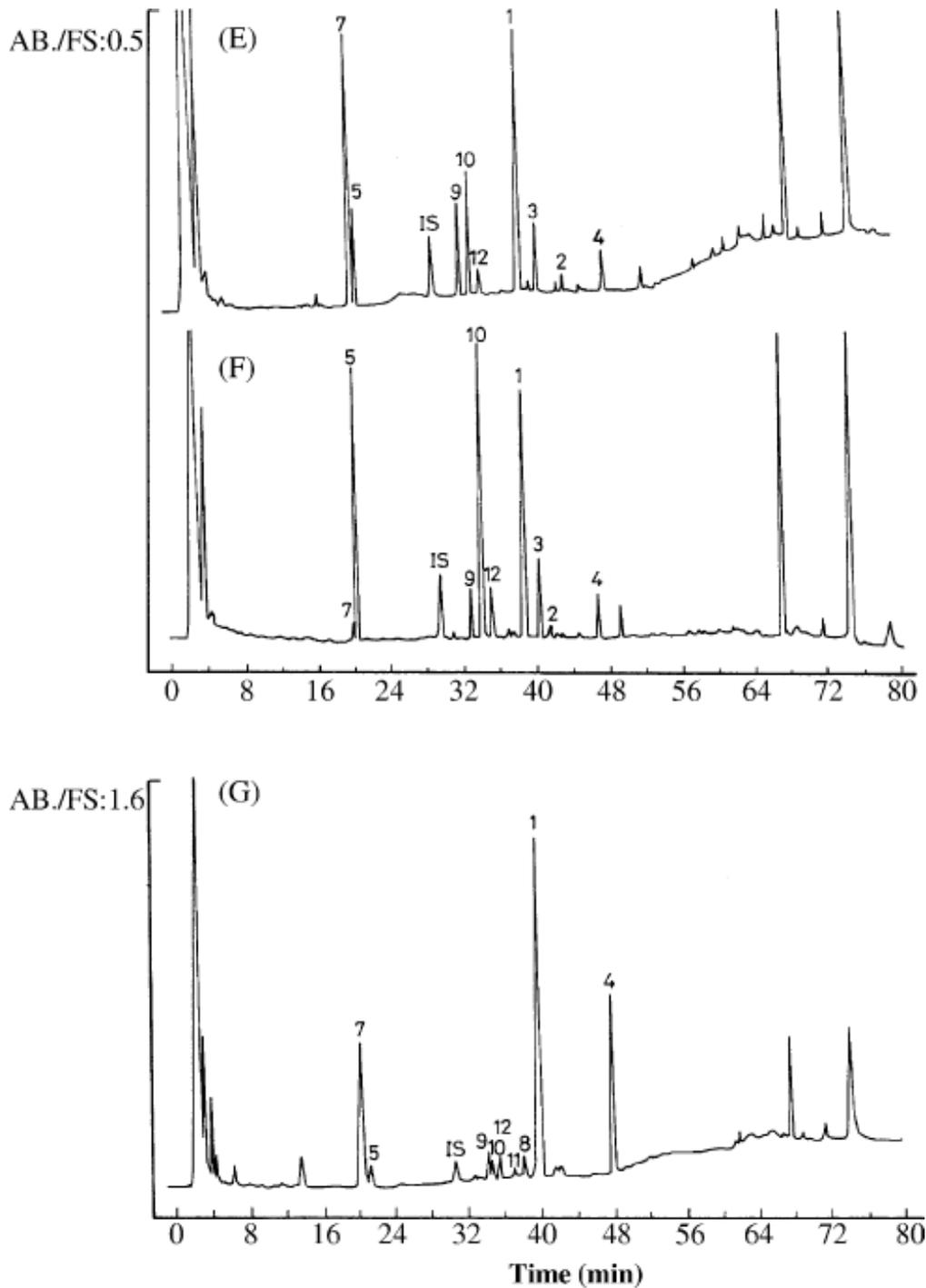
very sensitive detection systems such as fluorescent detection, mass spectrometry (MS), electrochemical detection (ECD) etc. which will help to lower the limits of detection (LOD) and limits of quantification (LOQ). However, generally ultraviolet (UV) detection method is used for detecting and quantifying ginsenosides in herbal samples. Most studies use C18 column with water or phosphate buffers and acetonitrile mixtures as solvent system using isocratic or gradient elution mode [11].

Chemical characterization not only helps to detect adulteration, but also can help predict the efficacy of TCM medications by using structural activity relationship (SAR) data. Chuang et al. [12], did a comparative HPLC study of 37 different commercial samples of ginseng by qualitatively and quantitatively determining various ginsenosides (Rb1, Rb2, Rc, Re, Rd, Rg1, Rf, Rg2, Ro, and three malonyl derivatives m-Rb1, m-Rb2 and m-Rc) present in the samples. This study showed that the content of ginsenosides decreased in the order *P. notoginseng* > *P. quinquefolius* > root hair of *P. ginseng* > red and white ginseng. Red ginseng is produced by steaming and drying the roots of *P. ginseng*, whereas white ginseng is obtained from dried roots of *P.*

*ginseng*. This study also revealed a chemical difference between red and white ginseng (i.e., red ginseng did not contain malonyl ginsenosides). The steaming process possibly caused the degradation of malonyl ginsenosides in white ginseng which explains the absence of malonyl ginsenosides in the red ginseng. These types of chemical changes are very important in TCM because most of the TCM formulations are prepared by decoction method. Another significance of phytochemical quantification of TCM drugs is the ability to correlate the pharmacological properties with the chemical content. For example, the ratio of Rg1/Rb1 is much lower in *P. quinquefolius* compared to *P. ginseng*. It is believed that the Rg1/Rb1 ratio is related to the ethnopharmacological properties of ginseng [13]. It has been shown that Rb1 is a weak CNS depressant whereas Rg1 is a CNS stimulant. Thus, a higher Rg1/Rb1 ratio might be responsible for the 'cooling' or calming property of *P. quinquefolius*, while a higher Rg1/Rb1 ratio of *P. ginseng* might be responsible for its 'hot' or stimulating property [14].

Infrared spectroscopy and capillary electrophoresis (CE) techniques are also used to chemically characterize natural products used in TCM.





HPLC chromatograms of ginseng extracts. (A) white ginseng, (B) red ginseng, (C) Shihchu ginseng, (D) Asian ginseng hairy roots, (E) wild American ginseng, (F) cultivated American ginseng, (G) Sanchi ginseng. Peak's identity: (1) Rb1, (2) Rb2, (3) Rc, (4) Rd, (5) Re, (6) Rf, (7) Rg1, (8) Rg2, (9) Ro, (10) mRb1, (11) mRb2, (12) mRc.

(Source: Chuang et al., 1995).

Apart from physicochemical methods, lately biological methods have also been used to authenticate plant drugs including TCM drugs. One of the methods of authentication of plant-based drugs involves genetic analysis at the DNA level [3]. In the Ginseng example, as in other plant species, genetic differences exist between

different species. Genetic differences are more definitive than phenotypic difference such as morphology and chemical constitution. Therefore, genetic methods of identification are much more reliable than those based on traditional pharmacognostic methods (similar to identifying human beings using DNA fingerprinting rather

than based on external features). Random amplified polymorphic DNA (RAPD), DNA fingerprinting using multi-loci probes, restriction fragment length polymorphism (RFLP), amplified fragment length polymorphism (AFLP), and microsatellite marker technology are some of the techniques employed in genetic identification of natural products [3]. Although the DNA-based technologies are ideal for identifying individual products, it may be technically difficult to identify components in a complex TCM formulation. Nevertheless, these types of technologies may be a good start in the right direction for the authentication of TCM products.

Apart from physicochemical and biological methods, text-mining is another useful technique for collecting ethnopharmacological and pharmacognostic data on TCM drugs. Text-mining is a sub-field of data mining that helps to extract data from free-text and the internet [15]. Given the ancient nature of TCM and the complexities of its diagnostic methods and drug formulations, text-mining will prove to be very useful in gathering data on TCM.

A highly commendable study by Gao et al. [16], combined several techniques systematically to authenticate the identity of components and the efficacy of a simple (two- component) TCM formulation consisting of *Radix Astragali* and *Radix Angelicae Sinensis* (*Dang Gui Bu Xue Tang*). The investigators chose a simple TCM formulation and systematically studied the various components of the formulation and their pharmacological effects, eventually establishing a clear correlation between the components and the efficacy of the formulation. The future of TCM lies in systematic studies like this which can counter the major

criticisms faced by TCM.

## Conclusion

A lack of sufficient clinical evidence and difficulty in quality control are the major challenges faced by TCM. Another problem faced by herbal drugs in general is the absence of association between chemical marker compounds and pharmacological activity. Modern pharmacognosy, armed with several cutting-edge physicochemical techniques, is extremely useful in identifying and characterizing TCM drugs and formulations. The ethnopharmacological component of pharmacognosy will help in identifying the traditional use of TCM medications and guide the formulation of hypotheses that can be tested using modern pharmacological techniques and clinical trials. With advancements in science and medicine, the complexities and ambiguities presented by TCM philosophy and drugs to the Western world can be slowly eliminated and hopefully safe and efficacious medications proven by modern science can emerge from TCM.

## Acknowledgments

Authors thank their respective employers (SJ: West Haven Pharmacy and RR: Mohammed Bin Rashid University) for their support.

## Declaration of Interest Statement

Both authors have no financial or non-financial conflicts of interest to declare.

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