
AN INTRODUCTION TO FLAVONOIDS-A REVIEW

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Article Received: 14 December 2025, Article Revised: 02 January 2026, Published on: 21 January 2026

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DOI: <https://doi-doi.org/101555/ijarp.7135>

Earth is a planet dominated by plants. The green plant is fundamental to all other life. The Oxygen we breathe, the nutrients we consume, the fuels we burn and many of the most important materials we use were produced by plants.

Plants represent the first stage in the evolution of living things in the process of the growth of nature, plants multiplied in number, variety and types. Humanity has identified as many as 7.5 lakhs species of plants¹⁻⁵ on earth, of which 5 lakhs are classified as “higher plants” and 2.5 lakhs as “lower plants”.

The association between plant and man is an age-old process starting from human civilization. There has always been a race between nature and human knowledge. The plants sustain nature and nature sustains them. The interdependence of man and nature increases day by day. If human race makes sensible use of nature, posterity is bound to be prosperous.

Since their evolution, plants became primarily useful for mankind. Realization of the importance of plants in the welfare of humanity prompted their systematic study from different angles. Thus many plant species^{6,7} have been subjected to detailed scientific analysis over the years. Yet not more than 10% of all the plants could be analyzed and a vast majority still remains uninvestigated. The study continues in various fields and provides challenges to several groups of plant scientists.

India with its vast area from Kashmir to Kanyakumari and varying soil and climatic

conditions ranging from tropical to temperate has one of the world's richest Vegetations, comprising of about 1,30,000 species of plants belonging to 120 families to be aptly called "the Botanic Garden of the World" India has a rich heritage of indigenous drugs from the Vedic times. The Ayurvedic system of medicine is purely of Indian origin and development. More than 2400 remedies have been known from Indian medical flora. The remarkable properties and therapeutic uses of about 700 plant drugs have been recorded by ancient Indian scholars, viz sushruta, charaka and vagbhata before 1000 B.C. Sanskrit literature written by them contains information about morphological features of many medicinal plants, their geographical distribution condition of growth, the best season for their maximum potency as well as their toxic properties.

Another ancient system of medicine flourished in south India is the siddha system⁸⁻²⁵. This system was introduced by the siddhars. They were those who attained or achieved perfection or heavenly bliss. They were the greatest scientists of ancient times and men of culture, intellectual and spiritual faculties combined with super natural powers.

Among siddhars, there were eighteen Maha siddhars, viz, Nandi, Agasthiar, Mular, Punnakesar, Pulasthiar, Punaikannar, Idaikkadar, Bohar, Pulikaiesar, Karurar, Konganavar, Kalangi, Azukannar, Agappiar, Pampatti, Theraiar, Kudambaiyar, Sattainathar. They imparted in different periods of history, not only their knowledge of medicinal plants but also their philosophy to their students and successors.

According to siddhars school, the human body is composed of 96 tatwas, 72,000 blood vessels, 13,000 nerves, 10 main arteries and 10 vital airs (prana) in the form of a network. It is owing to the derangements of the three humours, the body becomes liable to 4448 diseases. There are medicinal plants in India to cure all the above diseases of mankind (sage Agasthya).

These siddhars did not only cure the dreadful diseases like cancer, leprosy etc. by simple herbal powders, but also attained the immortality by a plant medicine popularly called by them as "Muppu."

According to them "Muppu" is composed of three salts, separate from a medicinal plant and reunited, which rejuvenate the human body. Rejuvenation does not necessarily mean restoring youthfulness to the old, but it simply means the maintenance of youth without reaching old age, if youth is maintained it becomes immortality.

India like all other countries has made significant progress by a systematic scientific study of

these plant drugs from the pharmacological, chemical, pharmacognostical and clinical points of view during the past 65 years. This brought to the forefront a large number of herbs used in Indian indigenous system for their approval efficiently and administration in modern medicines.

Recognizing the importance of medicinal plants collaborative team work for a complete study of plant drugs has been encouraged by the Indian Council of Medical Research (ICMR) Central Council for Research in Ayurvedha and Siddha (CCRAS) and Council for Scientific and Industrial Research (CSIR). The results of various studies on Indian Medicinal plants are available²⁶⁻³⁷. Central Drug Research Institute (CDRI), Lucknow initiated programme from 1979 to investigate Indian plants which either had a reputation in folk medicine or whose extracts showed consistent biological activity when put to a broad biological screen. So far under this programme over 8000 species were screened and biological activity confirmed in about 650 plants³⁸.

Through investigation of siddhar's literature reveals that each and every plant contain both poisonous chemicals as well as medicinally useful chemicals. The medicinal property of the plant alone was retained, by treating this plant with other simple chemicals or some chemical methods to neutralize the poisonous effect of the plant. Moreover, siddhars have used a mixture of herbal powders in some fixed ratio than a single herbal powder.

The above studies provide further scope for undertaking research work in several directions. The phytochemicals both pharmacologically active and poisonous and their structural changes can be discovered. Besides, there are different results regarding the structural modifications of pharmacologically active phytochemicals obtainable by combining different herbal powders at various proportions. If the modern methods of investigation of medicinal plants in India with the newly developed scientific approach are applied, this type of research will provide for the discovery of new effective plant drugs.

Phytochemistry³⁹⁻⁴⁴, evolved from natural products chemistry is confined to the study of products elaborated by plants and it has developed as a distinct discipline between natural product organic chemistry and plant biochemistry in recent years. It deals with the study of chemical structures of plant constituents, their biosynthesis, metabolism, natural distribution and biological functions. The fact that only less than 10% of about 7.5 lakhs species of plants on earth has been investigated indicates the opportunity provided and challenges thrown open to phytochemist. The task of the phytochemist is compounded in accomplishing the characterization of very small quantity of the compounds isolable from plants. Phytochemistry also enjoys the application of modern research for the scientific

investigation of ancestral empirical knowledge. It has found wide and varying application in about all fields of life and civilization. Its direct involvement in the field of food and nutrition, agriculture medicine and cosmetics, is well known for years. Its contribution even in seemingly remote areas such as plant physiology, plant pathology, plant ecology, paleobotany, plant genetics, plant systematics and plant evolution has been increasingly felt. One of the more encouraging trends as phytochemistry continues to grow and develop as a scientific discipline is the wider and wider applications that are occurring in agriculture, horticulture and forestry⁴⁵.

Among the phytochemicals, the polyphenolics constitute a distinct group. They embrace a wide range of substances, which possesses in common an aromatic ring bearing one or more hydroxy substituents or their ether or glycoside derivatives. These compounds possess great structural diversity and are of widespread occurrence among the secondary metabolites. A further feature of this particular group of compounds is their ability to interact with primary metabolites such as polysaccharides and proteins.

Among the several thousands of naturally occurring poly phenolic compounds, the flavonoids are the largest and the most widespread. The term “flavonoid” was first applied about 48 years ago by Geissman and Hinreiner⁴⁶⁻⁴⁷ to embrace all those compounds whose structure is based on that of flavone (2-phenyl chromone) (I) having basic C₆-C₃-C₆ skeleton in common when the heterocyclic ring is reduced, it becomes flavan (2-phenyl chroman) (II), Flavone (I) consists of two benzene rings (A and B) joined together by a π -ring (ring C). The various classes of flavonoid compounds differ from one another only by the state of oxidation of this carbon link. There is a limitation to the number of structures commonly found in nature, which vary in their state of oxidation from flavan-3-ols (catechin) (III) to flavonols (3-hydroxy flavones) (IV) and anthocyanins (V). Flavanones (VI), flavanonols or dihydro flavonols (VII) and the flavan 3-4- diols (proanthocyanidins) (VIII) are also included in the flavonoids. It should be noted that there are also five classes of compounds (dihydro chalcones or 3-phenyl propiophenones) (IX) chalcones or phenyl styryl ketones (X) isoflavones or 3 phenyl chromones (XI) neoflavones or 4- phenyl coumarins (XII) and the aurones or 2-benzylidene-3-coumaranones (XIII) which do not actually possess the basic 2-phenyl chromone (I) skeleton, but are closely related both chemically and biosynthetically to other flavonoid types, that they are always included in the flavonoid group.

The individual compounds in each class are distinguished⁴⁸ mainly by the number and orientation of hydroxy and methoxy groups in the two benzene rings. These groups are usually arranged, reflecting the different biosynthetic origin of the two aromatic nuclei. Thus, in the A ring (I) of the majority of flavonoid compounds, hydroxy groups are distributed at either C-5 or C-7 or only at C-7 (C-5 and C-7 of flavone become C-2' and C-6' in dihydrochalcones and chalcones and C-4 and C-6 in aurones) and generally are unmethylated. This pattern of hydroxylation follows from the acetate or malonate origin of the ring. The B-ring (I) of flavonoids on the other hand is usually substituted either by one, two or three hydroxy or methoxy groups. The rarely methylated position is C-4' with often methylation at C-3' and C-5'. The rarely methylated position is C-4' with often methylation at C-3' and C-5'. The hydroxylation pattern of the B-ring thus resembles that found in commonly occurring cinnamic acid (XIV) and coumarins (XV) and reflects their common biosynthetic origin from prephenic acid and its congeners.

A comparison of the nature and position of various substituents at different carbons of the flavonoid skeleton has been made use of in arriving at certain generalizations⁴⁹ regarding structure and properties. Most of the flavonoids⁵⁰⁻⁵⁶ occurs naturally in conjugated form, usually bound to sugar, by a hemi acetal linkage. But their conjugation with inorganic sulfates or organic acids is not unusual. The sugar free compounds are referred to as aglycones and it is probable that in most cases they are formed as artefacts during the course of extraction, since most living tissues contain very active glycosides which can work even in the presence of high concentration of organic solvents. The presence of sugars in the molecule confers sap-solubility to the generally somewhat insoluble flavonoid compounds. In anthocyanins the sugar imparts stability to the aglycone. Stability conferred by glycosylation to flavonols is observed in 3-O-glycosides of quercetin and myricetin, which are not susceptible to oxidation catalyzed by phenolase unlike the corresponding aglycones, presumably because of steric reasons⁵⁷. More and more range of new glycosides are encountered in plants⁵⁸⁻⁶³. An increasing number of flavonoid glycosides carrying sugars in B- ring hydroxyls have been reported⁶⁴⁻⁶⁶. Conjugation of flavones and flavonols through glucose with organic acids like malonic acid and derivatives of cinnamic acids have also been reported⁶⁷⁻

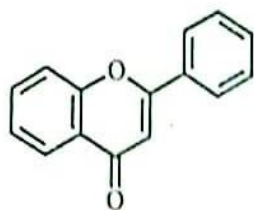
⁷⁰. The number of acylated flavonoid compounds succeeded by terpenoid counterparts^{71,72} is on the increase. As a result of electrophoretic studies, a number of zwitter ionic anthocyanins with malonic acid and succinic acid linked to C-6 of glucose have been isolated and

characterized⁷³.

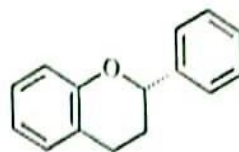
The sugars found in flavonoid glycosides include simple pentoses and hexoses (monosides) and di- and tri-saccharides (biosides and triosides) mostly combined through oxygen at C-1 position of sugars, usually by a α -linkage. In many cases, more than one phenolic hydroxyl group in the flavonoid molecule may be glycosylated giving rise to diglycosides and so on. The common sugars are D-glucose, D-galactose, L-rhamnose, D-xylose, L-arabinose and D-glucuronic acid. D-allose and D-galacturonic acid are rare and D-apiose is an unusual and uncommon one.

The study of the distribution of flavonoids in plants^{74,75} is continuing exercise and known flavonoids are being variation according to phyla, order, family and populational variation with in species have been detailed by Harborne and Turner⁷⁶. The presence of flavonoids in butterflies has been recognized⁷⁷ in 1983. In 1985, the distribution of flavonoids in animals has been reported with the isolation of 4'-methoxy flavone from scent glands of Canadian beaver (*Castor fiber*) and in Lepidoptera⁷⁸.

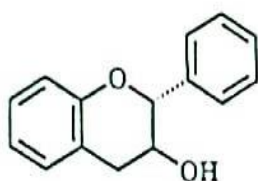
The review provides a Comprehensive overview of the Flavonoids, The compiled information further exploration, systematic investigation, and global recognition of Flavonoids for drug discovery and development. Additionally, the review may aid in identifying research gaps and promoting future studies. distinctive and systematic compilation of flavonoids. This compilation serves as a meaningful step toward bridging archival gaps and strengthening the foundation for future research in the field of phytochemistry.



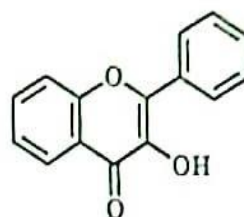
I Flavone



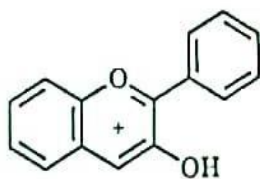
II Flavan



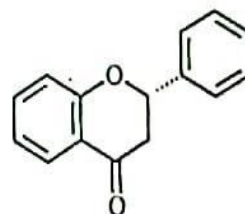
III Flavan 3-ol



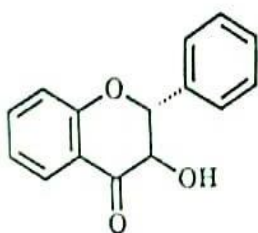
IV Flavonol



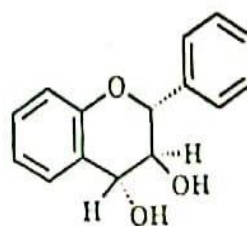
V Anthocyanidin



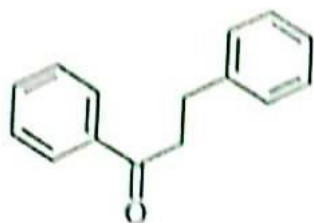
VI Flavanone



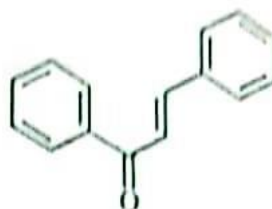
VII Dihydroflavonol



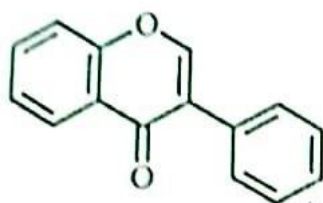
VIII Flavan 3,4-diol



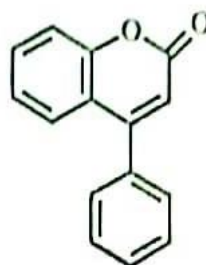
IX Dihydrochalcone



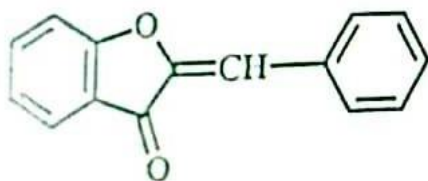
X Chalcone



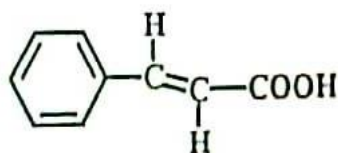
XI Isoflavone



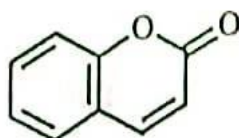
XII Neoflavone



XIII Aurone



XIV Cinnamic acid



XV Coumarin

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