The World Health Organization takes special interest in indigenous systems of medicines, particularly plant remedies. This is due to the fact that about 80 per cent of the world's population use herbal medicines and by the proper development of such systems only the organization's aim of providing "Health for all by 2000 A.D." is fulfilled.

The plant kingdom, no doubt, still holds many species of plants containing substances of medicinal value which are yet to be investigated; large number of plants are constantly being screened for their chemical and pharmacological properties. With the extermination of plant species progressing at an alarming rate in certain areas, even before the plant has been recorded, much less studied chemically, increased efforts directed towards the conservation of gene pools of locally used medicinal plants are urgent and most needed.

By the application of modern techniques of isolation and pharmacological evaluation, many new plant drugs find their way to medicine as purified substances rather than in the form of older galenical preparations. Chemical plant taxonomy, genetical studies involving secondary metabolites, tissue culture, the study of effects
of chemicals on plant metabolites and the induction of abnormal syntheses in plants are new areas pursued by an inter-disciplinary approach to develop new and more potent medicinal agents. The term 'medicinal phytochemistry' is synonymous with the interdisciplinary scientific approach to the development of drugs from plants.

Plants are considered to be medicinal if they possess pharmacological activities of possible therapeutic use. These activities are known generally as a result of continued methods of trial and error. With the increasing awareness of side effects like cytotoxicity, genotoxicity, etc., present day investigation in the discovery of new drug demands an array of strict systematic evaluation by a team of scientists drawn from a number of disciplines. There is no single philosophy that will lead to the discovery of new and more potent plant drug.

The contributions of natural products to medicine during the period after 1950 have been outstanding. Today emphasis of pharmaceutical research and development is on the creation of therapeutic, prophylactic and diagnostic substances with specific functions and minimum side effects in particular applications and here the plant derived substances have the advantage of being tool for modern medicine satisfying these conditions. Hence the latest trend
in the advanced countries indicates preference\textsuperscript{5} for natural drugs over synthetic ones. Similarly the desirability of a shift\textsuperscript{3} from synthetic chemicals to the natural products and their analogues in the safer utilizations of insecticides, pesticides, etc., is increasingly felt.

Another recent aspect of interest in plant drug research is the new concept of a non-specifically increased resistance (SNIR) of an animal to diseases attributable to other substances, besides the active principles responsible for specific biological activity\textsuperscript{6}. This probably justifies the use of many of the plant drugs as household remedies by natives of many countries from ancient times and hence warrants their evaluation in more detail.

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 approximately 130,000 species of plants belonging to about 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 strictly Indian in origin and development. More than 2400 remedies have been known from Indian medicinal flora. The remarkable properties and therapeutic uses of about 700 plant drugs have been recorded
by ancient Indian scholars - Sushrutha, Charaka and Vagbhatta - probably earlier than 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 toxic properties.

India, like all advanced countries, has also made significant progress by a systematic scientific study of these plant drugs from the pharmacognostical, chemical, pharmacological and clinical points of view during the past 50 years, bringing to the forefront a large number of herbs used in Indian indigenous system for their approved efficiency and administration in modern medicine. Recognising the importance of medicinal plants, collaborative teamwork for a complete study of plant drugs has been encouraged by the Indian Council of Medical Research (ICMR), Central Concil for Research in Ayurveda and Siddha (CCRAS) and the Council of Scientific and Industrial Research (CSIR). The results of various studies on Indian Medicinal Plants are available in as many as 7000 research publications and a number of books and monographs. Central Drug Research Institute (CDRI), Lucknow, initiated a programme from 1979, to investigate Indian plants which either had a reputation in folklore medicine or whose
extracts showed consistent biological activity when put to a broad biological screen. So far under this programme over 3000 species have been screened; biological activities have been confirmed in about 415 plants19.

A few of the notable contributions made in Indian plant products during the past twenty five years include the work on the alkaloids of Piper species20, Ancistrocladus heyneanus21, Cocculus laurifolius22, Murraya koenigii23, Tylophora asthmatica24, Alstonia scholaris25 and Phyllanthus niruri26, oxygen heterocycles of Seseli sibiricum27, Garcinia morella28, Artocarpus species29-31 and Mollugo species32-33, terpenoids from Aquillaria gallocha34, Zingiber zerumbet35, Commiphora mukul36, Ailanthus malabarica37, Cleistanthus collinus38 and Thevetia nerifolia39, withanolides from Withania species40, physalins from Physalis species41-42 and saponins and sapogenins from variety of plants43-45. Triterpenoid saponins isolated during the period 1987 to mid 1989 together with their occurrence, available physical and spectroscopic data and biological activity were reviewed by Mahato and Nandy46. Srivastava and Kulshreshtha reviewed the biologically active polysaccharides isolated from natural sources during 1977 to 1988. Also latest reports on new medicinal plants and / or additional information have appeared recently48,49. Detailed bibliography in respect of a number of medicinal plants
covering pharmacognosy, physiology, pharmacology, phytochemistry and utilization has been regularly reported in Medicinal and Aromatic Plant Abstracts (MAPA); so far 58 plants have been covered.

Phytochemistry, 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 products 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 6 per cent of about six lakhs species of plants on earth has been investigated, indicates the opportunity provided and challenges thrown to phytochemists. 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 almost all fields of life and civilization. Its direct involvement in the field of food and nutrition, agriculture and medicine and cosmetics is well known for years. Its contribution even in seemingly remote areas such as plant physiology, plant pathology, plant ecology, palaeobotany, plant genetics,
plant systematics and plant evolution has been increasingly felt.

Among the phytochemicals, the polyphenolics constitute a distinct group. They embrace a wide range of substances which possess 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 phenolic compounds, the flavonoids are the largest and the most widespread. Though the flavonoids have been found along with alkaloids, steroids, etc., not much attention was paid to their medicinal importance for a long time. Considerable interest has now been shown in plant flavonoids as human dietary components, therapeutic agents and as having significant activity in a variety of isolated animal cell system. Flavonoids have definite advantage over alkaloids from the point of view of pharmacological evaluation that they occur universally making a search for new active substances simpler and the overall uniformity in their chemical structures providing easier understanding of Structure-Activity Relationship (SAR). The ready availability of many
of the more common flavonoids in pure form is a definite advantage for the study of their biological activity and evaluation of their pharmacological properties. More than 3000 flavonoids have been characterised till now and new structures are being reported at an everincreasing rate. Flavonoids have attracted the attention of scientists of different disciplines and the systematic investigation on their occurrence, natural distribution, chemical nature and biological functions continues unabated.\textsuperscript{58-64}

The term 'flavonoid' was first applied about forty years ago by Geissman and Hinreiner\textsuperscript{65-66} to embrace all those compounds whose structure is based on that of flavone (2-phenylchromone) (I) having a basic C\textsubscript{6}-C\textsubscript{3}-C\textsubscript{6} skeleton in common. When the heterocyclic ring is reduced, it becomes flavan (2-phenylchroman) (II). Flavone (I) consists of two benzene rings (ring A and B) joined together by a three carbon link which is formed into a \textit{γ}-pyrone 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), flavanones or dihydroflavonols (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 (dihydrochalcones 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-benzylidine-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 within each class are distinguished mainly by the number and orientation of hydroxyl and methoxyl groups distributed in the two benzene rings. These groups are usually arranged in restricted pattern in the molecule, reflecting the different biosynthetic origins 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 and 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 the flavonoids on the otherhand is usually substituted by either one, two or three hydroxyl or methoxyl groups. The rarely methylated position is C-4' with often methylation at
I. FLAVONE

II. FLAVAN

III. FLAVAN-3-ol

IV. FLAVONOL

V. ANTHOCYANIDIN

VI. FLAVANONE
VII. DIHYDROFLAVONOLS

VIII. FLAVAN - 3,4-diol

IX. DIHYDROCHALCONE

X. CHALCONE

XI. ISOFLAVONES

XII. NEOFLAVONES
XIII. AURONE

XIV. CINNAMIC ACID

XV. COUMARIN
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.

Most of the flavonoids occur naturally in conjugated form, usually bound to sugar, by a hemiacetal linkage. But their conjugation with inorganic sulphates 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 glycosidases 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 aglycones. Stability conferred by glycosylation to flavonols is observed in 3-0-glycosides of quercetin and myricetin which are not susceptible to oxidation catalysed by phenolase unlike the corresponding aglycones, presumably because of steric reasons. More and more range of new glycosides are encountered in plants. An increasing number of flavonoid glycosides carrying sugars in B ring hydroxyls have been reported. Conjugation of flavones and flavonols through glucose with organic acids like malonic
acid and derivatives of cinnamic acids have also been reported\textsuperscript{69-70}. As a result of electrophoretic studies, a number of zwitter ionic anthocyanins with malonic acid and succinic acids linked to C-6 of glucose have been isolated and characterized\textsuperscript{71}. 

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 $\beta$-linkage. In many cases, more than one phenolic hydroxyl group in the flavonoid molecule may be glycosylated giving rise to di-glycosides 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\textsuperscript{58,59,72} is a continuing exercise and known flavonoids are being regularly discovered from new sources. Flavonoids are universal in vascular plants, but variation according to phyla, order, family and populational variation within species has been detailed by Harborne and Turner\textsuperscript{73}. 

Only in 1985, the distribution of flavonoids in animals has been reported\textsuperscript{74} with isolation of 4'-methoxy-flavone from scent glands of Canadian beaver (caster feber)
and in Lepidoptera; no doubt, the presence of flavonoids in butterflies has been earlier recognised.

A single plant may contain one or more aglycones with several glycosidic combinations. For this reason, it is better to examine the aglycones of acid hydrolysis of the plant extract before examining the nature of the glycosides. Flavonoids being polyphenolic give characteristic colour changes when treated with alcoholic \( \text{Fe}^{3+} \), ammonia vapour or alkalis. Positive Shinoda test \((\text{Mg-HCl})\) and formation of coloured complexes with heavy metal salts are characteristic of flavonoids.

Standard methods of extraction, separation and chemical characterization of flavonoid compounds are described by Peach and Tracey as well as Harborne. Systematic procedure for their identification employing chromatographic methods of analysis and chemical and spectral methods of identification have been detailed by Geissman, Mabry et al., Markham, Jay et al., Harborne and Mabry, and Linskens and Jackson.

The conventional chromatographic methods like column, paper and thin layer are still in use for the separation and purification of the flavonoid compounds. Increase in speed and efficiency in the separation of mixtures by new techniques like centrifugal TLC (chromatotron,
CTLC$^{81}$ and high pressure liquid chromatography (HPLC)$^{80-82}$ have been achieved. Flash chromatography or in combination with centrifugal TLC, column chromatography (on polyamide and on sephadex LH20) and low pressure liquid chromatography$^{83}$ are often used to separate samples weighing 100 mg to 10 gm in less than half an hour. For difficult separations requiring very high resolution semipreparatory HPLC with automatic fraction collector is an ideal method. Reverse phase chromatography$^{84}$ on chemically bonded phases gives best results for the separation of plant phenolics. The complication of irreversible absorption and decomposition of the solute at the liquid-solid interface in all techniques employing a solid stationary phase and liquid phase, is overcome by various support free liquid-liquid partition techniques. Among these, droplet counter-current chromatography$^{85-86}$ (DCCC) and rotation locular counter-current chromatography$^{87}$ (RLCCC) have found wide application in the field of flavonoids and other polyphenolics. However, the constant need in natural products chemistry to separate large and small quantities of complex mixtures efficiently and rapidly is unfortunately seldom satisfied by the use of any one chromatographic technique. The best results have been obtained by a combination of several techniques which are often complementary$^{88}$. Paper electrophoresis is a technique of limited application in flavonoid
analysis since, to be mobile, a flavonoid must be in an ionized state at the pH of the electrolyte. Its useful application lies in the recognition and identification of flavonoid sulphates\textsuperscript{89,90} and in the distinction of glycuronides from glycosides\textsuperscript{91}. Relative mobilities of different flavonoid sulphates are listed by Hostettmann\textsuperscript{83}. Electrophoresis finds greater application in the field of anthocyanins and betacyanins.

The flavonoid, once isolated as a homogeneous compound is characterized by the specific colour tests, physical constants, elemental analysis, $R_f$ values in various solvent systems, analysis of hydrolysis products, preparation of derivatives and comparison of these data with related compounds. Further support for confirmation of the structure of a flavonoid is achieved by the analysis of different spectral data (UV - Visible, IR, $^1$H and $^13$C NMR and MS).

The developments, in the general methodology of natural products chemistry\textsuperscript{92} is readily applicable to flavonoid compounds also. Ultra Violet-Visible spectroscopy is still one of the useful techniques available for flavonoid structural elucidation. The UV spectrum in methanol and with various diagnostic shift reagents give information about the type of flavonoids, oxygenation pattern and substitution. The use of $\text{AlCl}_3$ and $\text{AlCl}_3/\text{HCl}$ UV spectra in the
precise determination of the structure of flavonoid compounds was demonstrated by Voirin\textsuperscript{93} and the limitation of NaOAc spectra in flavonoid analysis has been reported by Rosler et al\textsuperscript{94}. The infra-red spectra\textsuperscript{95} provide information about the class of compound and nature of certain substituents. It is frequently used as finger print device for establishing the identity of two samples.

Over the past 30 years chiroptical methods like ORD and CD spectral analysis have been employed for the determination of stereochemistry of chiral flavonoids\textsuperscript{96,97}. The exciton chirality method\textsuperscript{98} employing the application of coupled oscillators in determining the chirality of natural products is receiving greater attention.

Mass spectrometry of flavonoids serves as a valuable aid in determining the molecular weight and probable structure even with very small sample size. The electron impact mass spectrometry (EIMS)\textsuperscript{99,100} is used for the volatile compounds; the nonvolatile compounds are converted to suitable derivatives like TMS ether, permethyl ether, methyl ester or similar derivatives. When two mass spectrometers are linked in tandem, it has now become possible to employ the first as separator and the second as analyser to perform direct mixture analysis (TANDEM-MS). This multiple stage mass spectrometry has been reviewed by Roush et al\textsuperscript{101}. 
Field desorption mass spectrometry (FD-MS) employed for polar and thermolabile compounds like flavonoids has been reviewed by Schulten and Games. Desorption chemical ionisation mass spectrometry (DCI-MS) using electrically heated tungsten probe and fast atom bombardment mass spectrometry (FAB-MS) using the sample solubilized in polar matrix (like glycerol, thioglycerol, etc.,) deposited in a copper target which is bombarded with energized neutral atoms to induce ionization and desorption appears to be the most advantageous one for the analysis of flavonoid glycosides. In the chemical ionization mass spectrometry (CI-MS) the ions are formed in ion-molecular collisions which include abstraction as primary process using weak gas phases like CH$_4$, NH$_3$, i-C$_4$H$_{10}$ in positive CI for protonation. In negative CI, OMe$^-$ as reagent for proton abstraction or Cl$^-$ as an attachment reagent is employed. The MS analysis of permethyl ether of glycosides is widely employed for settling structural problems in C-glycosyl flavones. Pyrolysis chemical ionization mass spectrometry of flavonoids under positive and negative ionization conditions is observed to yield data characteristic of both aglycone and sugar residues, providing an alternative for FD and FABMS techniques. The easy differentiation of flavanones and dihydroflavonols by the characteristic fragments has been reported. The
application of GC-MS\textsuperscript{111} analysis to perdeuteromethylated derivatives of flavonoids\textsuperscript{112} has rendered the identification of certain methoxylated compounds easier. Online HPLC-MS\textsuperscript{112} will be readily accepted by flavonoid researchers. Solution phase secondary ion mass spectrometry\textsuperscript{113} has been proved useful in the determination of the molecular weight of complex flavonoid glycosides. Becchi and Fraisse\textsuperscript{114} have reported mass-analysed ion kinetic energy (MIKE) and collision activated dissociation MIKE spectra of flavonoids providing characteristic fragment ions which permit differentiation of the 6- and/or 8- substituent location and the position of O-glycosylation.

The proton magnetic resonance spectroscopy is the established non-destructive method of flavonoid analysis. Use of high field magnets and computer assistance has made the recording of high resolution $^1$H NMR spectra of minute quantity of flavonoids\textsuperscript{115,116}. Shift reagents provide a method of spreading out PMR absorption signals. The use of lanthanide shift reagents in positioning of methoxyl groups of flavonoids was reported by Joseph-Nathan et al\textsuperscript{117}.

Of late, $^{13}$C NMR spectroscopy\textsuperscript{118-124} has become the most useful technique for the structural determination of flavonoids. $^{13}$C resonance signals extending over 200 ppm provide the nature of the carbon skeleton. Carbon relaxation time measurement being less difficult is very useful in
differtiating otherwise nondiscernable carbon atoms like C-6 and C-8 in flavonoids. Interglycosidic linkages in the case of disaccharides\textsuperscript{125} (rutinose, neohesperidose, etc.,) type of linkage with aglycone and sugars and conjugation with sulphates and acids can also be determined. Homonuclear and heteronuclear correlation spectroscopy\textsuperscript{126} (HOMCOR and HETCOR) and the various decoupling experiments have reduced the difficulty in the interpretation of \textsuperscript{1}H and \textsuperscript{13}C NMR spectra of complex molecules. Fourier transform NMR employing popular pulse sequences like off-resonance, heteronuclear decoupling, gated heteronuclear decoupling, inverse gated heteronuclear decoupling and slective proton decoupling has eased the task of assignment of peaks in a \textsuperscript{13}C NMR spectrum. Refocussed INEPT with decoupling is an alternate of off-resonance decoupling for assigning carbon multiplets. J-modulated spin echo spectroscoby\textsuperscript{127} is yet another method of off-resonance decoupling which gives positive signal for carbon with even number of hydrogen (CH\textsubscript{2} and quarternary) and negative signal for carbon with odd number of hydrogen (CH and CH\textsubscript{3}) attached. The flavonoid glycoside from violet blue flowers of \textbf{Primula polyantha} was completely charac-
terized as quercetin 3-0 (β-D-glucopyranosyl (1 → 2)-β-D-
glucopyranosyl (1 → 6)-β-D-glucopyranoside) by 2D-NMR methods\textsuperscript{128}. Also the structures of a few cytotoxic flavo-
noids were established unambiguously with NMR assignments
based on $^1H-^1H$ COSY, $^1H-^{13}C$ HETCOR and selective INEPT experiments$^{129}$.

If the flavonoid compounds can be obtained in a fine crystalline form, X-ray analysis can help in further confirming the structure as reported in the case of calycop-terin$^{130}$.

Final confirmation is always desired to be established by unequivocal total synthesis. The conventional methods of synthesis of flavonoids from simple precursors by condensation methods have been proposed by Baker and Venkataraman$^{131}$, Allan and Robinson$^{132}$ and Algar and Flynn$^{133}$. These methods of synthesis have been modified by Farkas et al.$^{134}$ and Wagner et al.$^{135}$ as illustrated by the synthesis of a number of flavonoids and their methyl ethers. Many flavonoid compounds have been prepared by simple modification of the existing structure through nuclear oxidation, nuclear reduction, isomerization, selective alkylation and dealkylation, selective glycosylation and partial hydrolysis. Farkas et al.$^{136}$ accomplished the synthesis of methoxylated flavones from the corresponding brominated methoxy chalcones. The synthesis of 5,6,7,3',4'-pentamethoxyflavone (sinensetin) by dehydrogenation of the corresponding flavone with selenium dioxide has been achieved by Wagner et al.$^{137}$. This flavone has been used as the starting material
for the synthesis of a number of related flavones. Bose et
al\textsuperscript{138} have reported cyclization and simultaneous dehydration
of the hydroxy chalcones to the corresponding flavones by
heating with palladium on charcoal.

The synthesis of flavonoid glycosides have been
achieved using the \( \alpha \)-acetobromo sugars of pentoses, hexoses
or disaccharides and the aglycones in the presence of cata-
lysts. The selective glycosylation of 7-OH has been achieved
by Zemplen and Farkas\textsuperscript{139}. Synthesis of other glycosides
have been accomplished by transacylation methods by Nograri
et al\textsuperscript{140} and Wagner et al\textsuperscript{141}. The total synthesis of C-
glycosyl flavones has been reported by Eade et al\textsuperscript{142}. A
more general synthesis, exemplified by the preparation of
5,7,4'–trimethoxy vitexin\textsuperscript{143} and other complex ones has been
provided by later workers\textsuperscript{144}. Thus the synthesis of almost
all types of mono and di-C-glycosyl flavones and flavone C-
glycosyl–O-glycosides has been accomplished\textsuperscript{145}; synthesis of
some novel flavonoids has been illustrated by Rakosi et
al\textsuperscript{146}. The chiron approach to the total synthesis of
natural products\textsuperscript{147} might become a useful guide in the
synthesis of chiral flavonoid compounds. Recently, studies
of the selective O-alkylation and dealkylation of flavonoids
with anhydrous aluminium bromide were reported by Horie et
al\textsuperscript{148}. 
Great progress has been made in the bio-synthesis of flavonoids. Our present knowledge in flavonoid biosynthesis is based on a combination of earlier results from radioactive tracer studies in vivo and the more recent data obtained at the enzyme level in vitro. In the past few years the enzymology of flavonoid biosynthesis has made particularly rapid progress. Flavonoid biosynthesis can be considered in three stages. The first is the formation of the basic C₆-C₃-C₆ skeleton through acetate-malonate and shikimic acid pathway to aromatic compounds. The second state is concerned with the ways by which the different classes of flavonoids are synthesized. The final stage embraces the elaboration of individual compounds within each flavonoid class, involving steps such as hydroxylation, glycosylation, methylation, etc. Chalcone is considered as the common intermediate in the biosynthesis of all classes of flavonoids. Insight into all three aspects of the problem of flavonoid biosynthesis has come in the past from comparative anatomy and chemical genetic studies and recently from feeding experiments with radioactive tracers. Major work on chemical genetic studies have been carried out by Grisebach and co-workers. Recent research has led to the isolation and characterization of enzymes of the pathway of flavonoid biosynthesis. The use of young plant tissues and cell suspension cultures as
source materials has also greatly facilitated the study of flavonoid biosynthesis at the enzymic level. Roux and Ferreira\textsuperscript{159} have highlighted the special role of $\alpha$-hydroxy chalcone as the key intermediate in flavonoid biogenesis. A comprehensive report on the biosynthesis of flavonoids by Manitto\textsuperscript{160}, a good account of biosynthesis of shikimate derived phenolic compounds by Harborne\textsuperscript{161}, biosynthetic studies \textit{in vivo} with labelled precursors and biochemistry of flavonoid biosynthesis by Heller\textsuperscript{162} are useful publications. The importance of flavonoids and other secondary metabolites in plant biochemistry has been detailed in "The Biochemistry of Plants"\textsuperscript{163}. Different aspects of mammalian metabolism of flavonoid compounds have been reviewed by DeEds\textsuperscript{164}, Scheline\textsuperscript{165} and Griffiths\textsuperscript{166}. Flavonoids are constituents of the mammalian diet derived from plants. The ingestion of flavonoids by mammals, in the diet or for therapeutic use, brings them in contact with both intestinal microorganisms and mammalian tissues which are capable of biotransformation of flavonoid compounds. The available evidences indicate\textsuperscript{166,167} that the hydrolysis of flavonoid glycosides to their corresponding aglycones, ring fission and oxidative and reductive transformations are mediated by intestinal microorganisms. Though it is certain that the metabolic changes undergone by flavonoids occur within mammalian tissues, the relative contribution of individual tissues is not fully understood.
The flavonoids find exceptional use as taxonomic guide in the classification of plants. The reason for preferring flavonoids to other secondary metabolites is their structural diversity, widespread distribution, comparative stability, easy detection and identification and the fact that this group of plant products is not actively concerned with cellular metabolic processes. Any particular flavonoid can be relied to be present in more or less constant amount in the same tissue of the same species so long as the plants are grown under normal physiological condition. The conspicuous exception to this is the variation in the relative concentrations of p-coumaric acid and caffeic acid (mono- and dihydroxyphenyl propanoid precursors) as well as kempferol and quercetin which are insignificant from the taxonomic point of view. Importance of flavonoids in chemotaxonomy can be illustrated with a few examples. Phloretin or its 3-hydroxy derivatives occur in all species of *Malus* (Rosaceae)\(^{168}\). No other genus in Rosaceae contain these compounds. Caviunin, an isoflavone is a taxonomic marker in *Dalbergia* species\(^{169}\). Quercitrin, the major constituent in the parasite *Dendropthoe falcata* (Loranthaceae) growing on plants of different families projects its possible use as a chemotaxonomic marker\(^{170}\) of this species. The flavonoid profile characterized by C-glycosyl flavones of *Mollugo* species\(^{171}\) supported its
separation from Aizoaceae of the Centrospermae and placement in Molluginaceae along with Caryophyllaceae in Caryophyllales. Among the numerous flavonoids of higher plants the rare and unusual ones find more acceptance in micromolecular taxonomy. Quite recently a survey of 2'-oxygenated flavonoids along with their possible biosynthetic pathways has been presented. \(^{172}\)

Flavonoids are multifunctional and the function varies according to the need and stress placed upon the plant and depending on its stage of growth and development. The most significant function of the sap-soluble flavonoids is their ability to impart colour to the plants in which they occur. They are mostly responsible for the orange, scarlet, crimson, mauve, violet and blue colours as well as contributing much to yellow, ivory and cream shades. Brown and black pigments found in nature are either due to the products of oxidation of flavonoids and related phenolic compounds or to their chelates with metals. Anthocyanin-flavone glycoside copigment complexes \(^{173}\) are stabilized by chelation with metal ions or by H-bonding \(^{174}\). These copigments are found to protect the anthocyanins in vivo from nucleophilic attacks resulting in colour loss. Carotenoids and chlorophylls are the other colouring materials in higher plants. The anthocyanins serve as anti-microbial agent, effective growth inhibitors and in pollination ecology and
seed dispersal by attracting insects and animals. Both fruit and flower colours provide immense aesthetic pleasure; conscious selection of colour varieties among garden plants and horticultural crops has been in practice for a long time. Further, in vivo studies of anthocyanins show that acylation with hydroxy cinnamic acids and dibasic acids like malonic acid and succinic acid stabilises anthocyanins and significantly protects them from photooxidative degradation. The important functions of flavonoids in plants are their protective role as light screen against damaging UV radiation, as feeding deterrents and protection from herbivores and as allelopathic agents. In biological systems, the stimulation of protein degradation as well as inhibition of protein formation by antibiotics resulted in the flavonoid accumulation implicating the importance of flavonoids in protein synthesis. Other important functions, include their role as anti-oxidants, enzyme inhibitors, precursors of toxic substances and as phtosensitizing and energy transferring compounds, in control of plant growth and development, in respiration, photosynthesis, morphogenesis and sex determination in plants.

Apart from the physical and morphological means, chemical means are a major method of plant defence. A significant range of flavonoids have been encountered as antifungal agents. A number of flavonoids are being induced
in plants following fungal invasion. Some of the flavonoids affect the behaviour, growth and development of insects due to their toxicity, while flavone glycosides are feeding stimulants\textsuperscript{180}. The metabolic challenges of the plant flavonoids including the condensed tannins to the insects consists mainly of the variety of phenolic groups. This activity is destroyed when the phenolic OH group is methylated in flavonoids. The structure-activity effects have been studied for a number of flavonoids for anti-growth and antibacterial activity and it has been found that growth inhibiting activity depends on the presence of orthodihydroxy group in ring A and B and not the functional group of ring C and the position of the ring B (at C-2 or C-3 as in flavones or isoflavones). The glycosylation of flavonoids also show marked variation in growth inhibition; 3-O-glycosylation inhibits growth but not 7-O-glycosylation. The enhanced activity of flavanones compared to the corresponding flavones showed that the coplanarity of the flavonoid rings of flavones may hinder their biological efficacy. Different types of bio-assay involving several types of organisms conducted with isoflavonoid phytoalexins by Smith\textsuperscript{181} revealed that they possessed fungitoxicity and limited antibacterial activity. The introduction of isoflavonoid phytoalexins in plants causes phytotoxicity\textsuperscript{182,183} such as inhibition of respiration, reduced growth of suspension
cultures, repressed seed germination, retarded root growth and electrolytic leakage.

The occurrence and concentration of flavonoids in food stuff have been reviewed by H"armann\textsuperscript{184}. The chemically modified anthocyanins have found increasing use as approved colours in formulated food and beverages. Although different groups of flavonoids are consumed, the diversity is removed by intestinal micro organisms hydrolysing the glycosides. The flavonoids combine with dietary proteins and carbohydrates and with digestive enzymes and cellular components of the digestive tract. A small fraction of the flavonoid is absorbed into the blood stream and the unabsorbed compounds affect many aspects of digestion and health.

An ever-increasing number of pharmacological effects of flavonoids have become known during the past fifty years through the discovery of new plant flavonoids and their derivatives\textsuperscript{63,64}. The spasmylytic, antianginal, antiulcer, antihepatotoxic, antiinflammatory, antiallergic, antimicrobial and antiviral effects of flavonoids are noteworthy. In recent years a number of flavonoids like baicalin, taxifolin, gossypin, proanthocyanidins, nepetrin, diosmin, fisetin, sophoricoside, (+)-catechin, (-)-epicatechin and 5,7-dimethoxy flavone have been reported to have antiinflammatory effects\textsuperscript{186-188}. Recently the effect of
flavonoids on arachidonate metabolism was reported by Ferrandiz et al. Many semisynthetic flavonoid derivatives also show this effect of which (O-β-hydroxy ethyl) rutin and various quercetin derivatives are important. Studies of compounds with flavone skeleton were stimulated by recognition of antiallergic effects. Thus, orally effective antiallergic chromone drugs (kellin, hypolaetin-8-glycoside disodium chromoglycosate, etc) are recently in use. Anti-viral activity of a few flavonoids were investigated by Pusztai et al. and observed that hydroxylation in 3-position appears to be a prerequisite for this activity. Anti-rhinovirus and anti-picornovirus activity of certain flavonoids have also been reported. Anti-cancer activity of a few flavonoids (flavones, isoflavones, flavanones and flavonols) are also reported. Recently 7,8-di-O-substituted flavans, biflavans and flavones showed cytotoxic activity and it has been established that the activity was due to methoxy and/or hydroxyl groups in the structure.

Inhibition of human immuno deficiency virus reverse transcriptase is currently considered a useful approach in the prophylaxis and intervention of Acquired Immuno Deficiency Syndrome (AIDS) and natural products have been extensively explored as inhibitors of this enzyme, to discover drugs active against AIDS. Recently 150 pure natural products have been examined and polyphenolic...
compounds were found to be responsible for the activity; among flavonoids tested quercetin exhibited moderate activity.

The antihepatotoxic effect of flavonoids was first demonstrated by Halm et al\textsuperscript{196} with the flavanolignan, silybin and its isomers. About thirteen flavonoids and coumarins have been demonstrated\textsuperscript{197} to be antihepatotoxic or liver protective agents. The screening of plants, recorded in Indian folk medicines, for liver injury has established\textsuperscript{198} that the active principles are flavonoids. Antiulcerogenic property of 3-0-methyl (+)-catechin, apigenin and luteolin, antidiabetic effects of hispidulin and nepetin and analgesic effects of puerarin are also reported\textsuperscript{199,200}.

Several dihydrochalone derivatives are used as sweeteners. The bitter taste of flavanones and their neohesperidosides, sweet taste of dihydrochalcone neohesperidosides, reduction of the bitter tastes of flavanone glycosides by flavones and the tastelessness of the flavone glycosides irrespective of the nature of sugars were elaborately studied by Horowitz and Gentili\textsuperscript{201}. Although flavonoids have been extensively studied in medicinal research for diverse physiological effects, their role in plants from which they are derived has not been unambiguously established.
Work on different aspects of flavonoids, including discovery of new compounds, biological activity, medicinal properties, etc., are regularly reviewed and the knowledge is updated through proceedings of regular international symposia on flavonoids. Considerable work on the chemistry and pharmacological properties of a number of flavonoids has been accomplished in the laboratories of our department.
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