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Review Article

FLAVONES AND THEIR DERIVATIVES: SYNTHETIC AND PHARMACOLOGICAL IMPORTANCE

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ABSTRACT

Flavones (from the Latin flavus, which means "yellow") are a kind of flavonoid with a backbone of 2-phenylchromen-4-one. Flavones, one of the most important classes of plant secondary metabolites, are well-known for their anti-cancer, anti-inflammatory, anti-microbial, antioxidant, anti-osteoporatic, anti-diabetic, anti-estrogenic, anti-allergic, and metal chelating properties. These family compounds have been intensively studied synthetically due to their wide spectrum of biological actions, and more than 4000 chemically distinct flavonoids have been identified from plants. However, new advances in synthetic chemistry have resulted in the production of a number of therapeutically important derivatives. This article summarizes the synthesis of flavones, their derivatives, and other flavone analogues which have the potential for treating a range of illnesses and ailments.

Keywords: Flavones, Flavones derivatives, Flavones synthesis, Flavones reaction, Pharmaceutical application.

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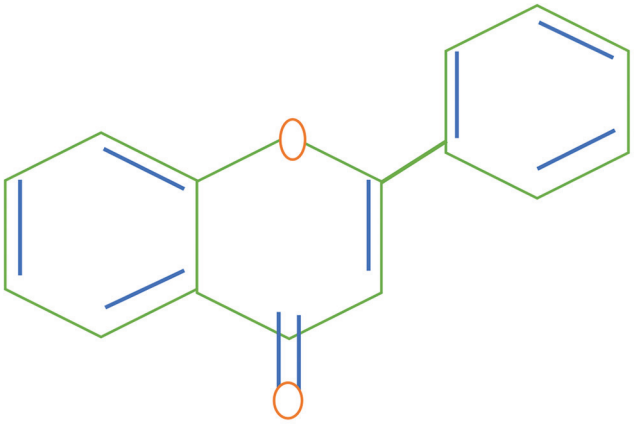
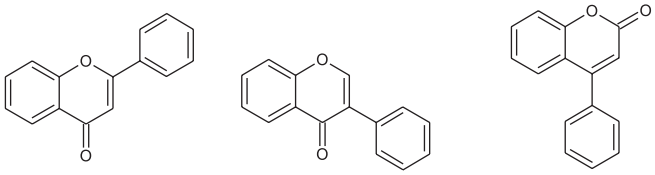
INTRODUCTION



Other flavonoids include isoflavonoids, which are produced from the 3-phenylchromen-4-one structure, and neoflavonoids, which are derived from the 4-phenylcoumarin structure. Anthoxanthins (flavones and flavonoids) are broadly dispersed in yellow plant pigments, because all three flavonoid families are ketone-containing molecules [1]. Flavone (2-phenylchromen) derivatives are heterocyclic compounds found in nature that belongs to the flavonoid family. By adding a heteroaryl moiety to the C-2 position of chromone derivatives, the biological activity of flavone has been increased [2].



Flavone Isoflavone Neoflavone

Flavones are a polyphenolic chemical found in plants that belong to a wide family. Tea, red wine, apple, tomato, cherry, onion, thyme, parsley, soybeans, and other legumes, grape, fruit, orange, lemon, ginkgo, and neem are all good sources of flavonoids in the form of flavonols, flavones, isoflavones, flavonones, and biflavones. Flavonoids have attracted the attention of synthetic chemists due to their wide distribution and low toxicity when compared to other chemical types of substances. Flavones limit proliferation with little or no damage to normal cells, according to research [3-5].

According to a literature review, chalcones and flavones are a class of chemicals that could be used to build low-cost anti-cancer, anti-inflammatory [6], anti-osteoporotic [7], anti-diabetic [8], and other agents in the future. Some examples are provided below in Fig. 1.

METHODS OF SYNTHESIS OF FLAVONES

Flavones can be synthesized in a number of different methods. Flavones are traditionally made through Baker-Venkatraman rearrangement and Claisen Schmidt condensation, which involves converting 2-hydroxyacetophenone to benzoyl esters, then rearrangement in base to 1,3-diphenylpropane 1,3-diones, which are then cyclized under acidic conditions to yield flavones. Under Claisen Schmidt conditions, hydroxychalcones produced from 2-hydroxyacetophenone and benzaldehyde can undergo oxidative cyclization to yield flavone rings (Fig. 2).

The following are some of the methods which have been used to prepare flavones.

From *o*-hydroxyacetophenone

Green chemistry is the order of the day, so it was decided to make some chalcones without utilizing solvents in an environmentally responsible manner. The Claisen-Schmidt reaction between acetophenone derivatives and substituted benzaldehydes in the presence of NaOH is used in the synthesis as a solvent-free solid state trituration technique. The remaining chalcones were supposed to be made using KOH as a basis. It was proposed to use dimethyl sulfoxide [DMSO]/I2 to synthesize several novel flavone derivatives from the matching chalcone employing these chalcone derivatives [9].

Methods

General procedure for the synthesis of substituted chalcone

Method 1

In a mortal pestle, around 24 mmol of aryl aldehyde (1,2 equivalent) was triturated with NaOH powder applied in portions with continuous

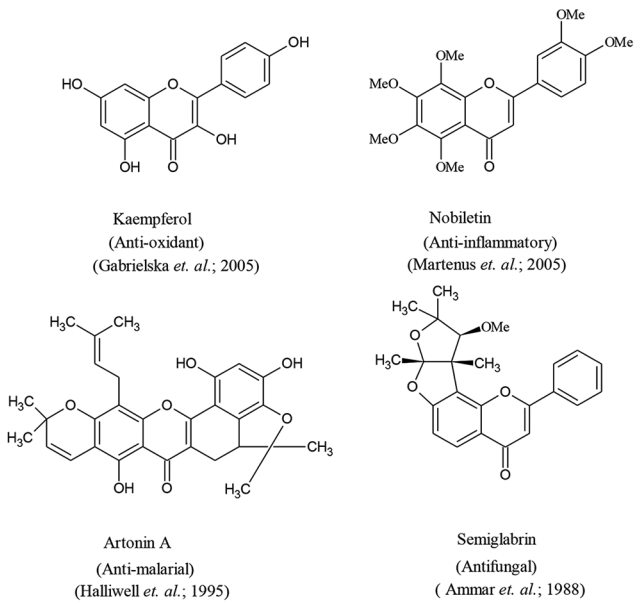


Fig. 1: Naturally occurring flavones with potent biological activities

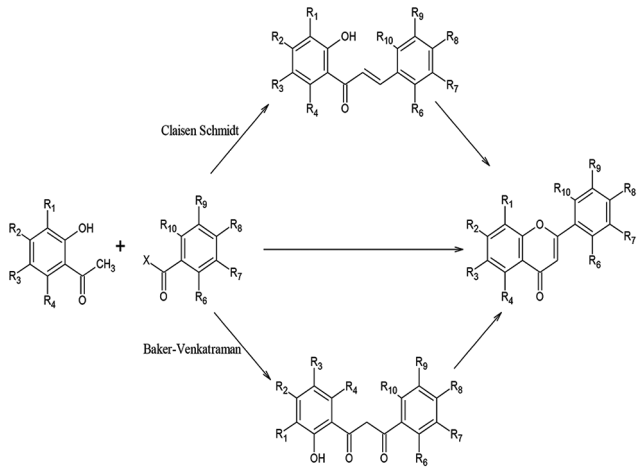


Fig. 2: Basic reactions for the synthesis of flavones

trituration. Continuous trituration was used to add 20 mmol 2-hydroxyacetophenone (1 equivalent). Continuous trituration resulted in the formation of a solid yellow mass. Thin-layer chromatography was used to observe the reaction. To obtain crude chalcone, the produced yellow solid was promptly washed with hot methanol.

Method 2

KOH pellet (3 equivalent) was added after 2-hydroxyacetophenone (1) (1 equivalent) and benzaldehyde (2) derivatives (1,2 equivalent) were dissolved in EtOH. TLC was used to show reaction complete after 6–12 h of stirring at room temperature. The liquid was placed onto crushed ice and acidified with dilute HCl once the reaction was worked up (pH=5). To obtain crystalline chalcone (3), the solid was recrystallized from dilute ethanol.

General procedure for the synthesis of all substituted flavones

In a radical basis function, 5 mmol of synthesized 2-hydroxy arylchalcone was introduced to 6 ml of DMSO. The reaction mixture was then heated on an oil bath at 110°C for 2–6 h with a catalytic quantity of I2. TLC showed that the reaction had finished. After working up the reaction, the fluid was placed onto crushed ice and the surplus I2 was eliminated by slowly adding sodium thiosulfate solution. To obtain crystalline flavone (4), the precipitated product was filtered by suction and the solid was recrystallized from dilute ethanol (Scheme 1).

From 2'-allyloxy-α, β-dibromochalcones

The use of iodine in the dimethylsulfoxide reagent to produce 2'-allyloxy-, -dibromochalcones (5), which lead to the equivalent 3-bromoflavones (6). When 2'-allyloxy chalcones were treated with DMSO-I2 reagent, the allyl group was removed easily, followed by cyclization and dehydrogenation, yielding flavones (7) [10].

Procedure for the synthesis of flavones

Iodine (1 mmol) was added to a solution of 2'-allyloxy-,-dibromochalcones (1 mmol) in DMSO (5 ml) and the reaction mixture was heated in an oil bath at 130°C for 30 min. Iodine was removed after cooling by washing with a saturated sodium thiosulfate and water solution. The product was then purified by column chromatography (hexane/ethyl acetate, 9:1) after being extracted with ethyl acetate (Scheme 2).

From 1,3-benzoxazine

A series of 6- and/or 8-substituted 1,3-benzoxazines with the flavone moiety at the 3-position has been produced. The compounds were made by reacting 6 or 8-substituted salicylaldehydes with aminoflavone, reducing them, and then cyclizing the resulting aminoflavone precursors with $CHCl_3$/HCHO to get the required 1,3-benzoxazine skeleton [11].

General procedure for the preparation of 6-(2H-1,3-benzoxazine-3(4H)-yl-2-phenyl-4H-chromen-4-one derivatives

Procedure: 6-[(1E)-(2-hydroxyphenyl) methylidene] amino-2-phenyl-4H-chromen-4-one (8) 6-aminoflavone (0.001 mol) was prepared in 20 ml ethanol and then transferred to a round bottom flask. The mixture was boiled in a water bath until it was completely dissolved. Salicylaldehyde (0.001 mol) was added drop-wise to the resultant mixture, which was then refluxed for 4 h. Schiff's base (8) was isolated, filtered, dried, and recrystallized from chloroform and petroleum ether (1:1) to yield orange microcrystalline powder (Scheme 3).

From salicylaldehyde and enolate

Sashidhara *et al*. recently succeeded in synthesizing flavone (4) using a process involving salicylaldehyde (9) and an enolate produced from acetophenone (10) (Scheme 4) [12]. To begin, Mazimba *et al*. reported that the Knoevenagel reaction of salicylaldehyde (9) and acetophenone (10) in the presence of KOH (aq.) in ethanol yielded chalcone (11) in 85% yield. In the presence of iodine and in a solvent-free environment, chalcone (11) was oxidatively cyclized to generate flavone (12) in a 72% yield. Methyl, methoxy, and chloro substituted acetophenones were likewise tolerated well in the process, yielding equivalent flavone yields.

From 2'-hydroxychalcone and vanadium pentoxide

According to Khan and Goswami, cyclization of 2'-hydroxychalcone (13) using a combination of vanadium pentoxide, hydrogen peroxide, and ammonium bromide in dichloromethane-water at 0–5°C, followed by dehydrobromination (14) of the brominated products using 0.2M ethanolic KOH solution at ice-bath temperature to form flavone (15) (Scheme 5) [13].

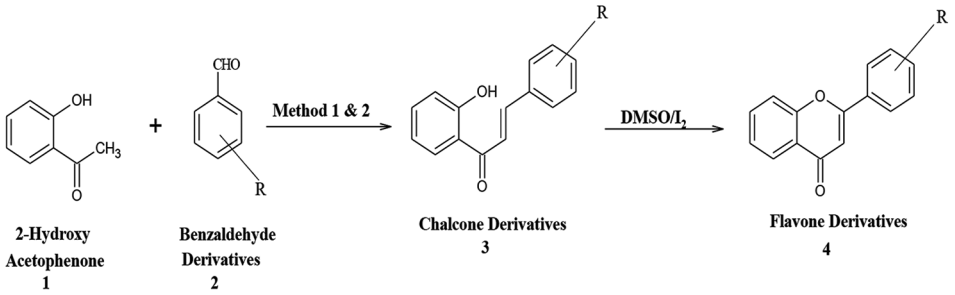
From silica gel supported $InBr_3$ or $InCl_3$ catalyst

Ahmed *et al.* [14] reported that silica gel supported $InBr_3$ or $InCl_3$ (15–20 mol %) was investigated as a new solid-support catalyst for the facile and efficient cyclization of 2'-hydroxychalcones (16) and flavanones (17) to yield the corresponding flavones in > 80% yield under solvent-free conditions (Scheme 6).

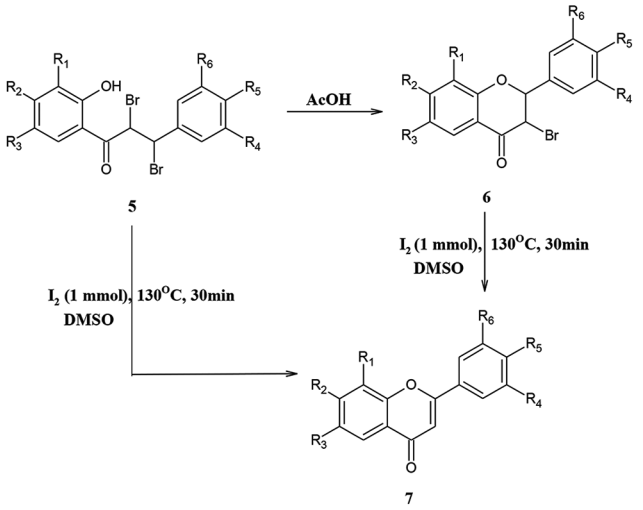
SUBSTITUTION REACTIONS

Alkylation reactions

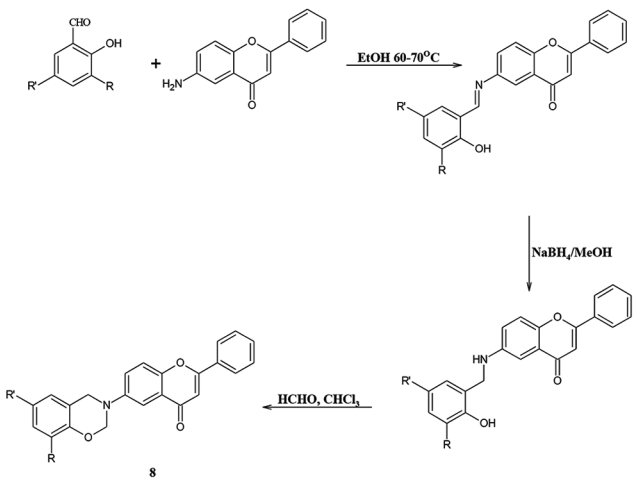
According to the approach shown in Scheme 7, 25 alkylated flavonoids were synthesized utilizing the building blocks baicalein (18),



Scheme 1: Synthesis of chalcones by trituration and conventional method and flavone. Method 1: Trituration method (Solid phase synthesis). Method 2: EtOH/KOH, Stirring at RT (6-12 hr)



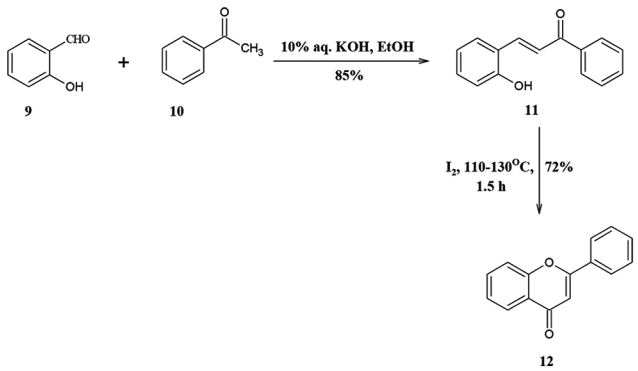
Scheme 2: Synthesis of flavones derivative from 2'-allyloxy-α, β-dibromochalcones



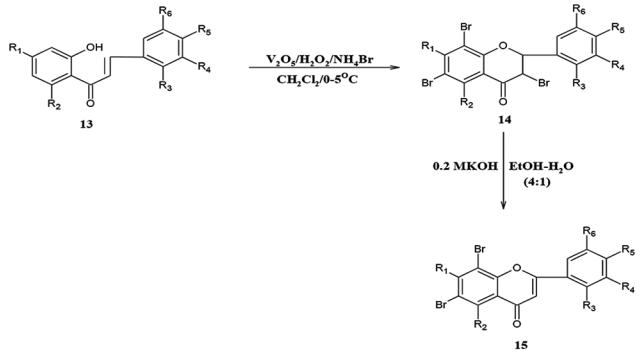
Scheme 3: Synthesis route of 6-(2H-1,3-benzoxazine-3(4H)-yl)-2-phenyl-4H-chromen-4-one derivatives

3,7-dihydroxyflavone (19), and chrysin (20). The synthesis method used MW irradiation to react the building block with the alkyl halide in the presence of anhydrous potassium carbonate.

Almost all alkylation reactions that used baicalein (18) as a building block yielded two alkylated derivatives. The main products were those



Scheme 4: Sashidhara and co-workers synthesis of flavones



Scheme 5: Synthesis of flavones derivative from 2'-hydroxychalcone and vanadium pentoxide

with one alkyl side chain on the oxygen at position 7 (21, 23, 24, 26, 28, and 30), with by-products including two alkoxy side chains on C-6 and C-7 (22, 25, 29, and 31). The reaction of baicalein (18) with alkyl iodide, on the other hand, yielded a mixture of two monoalkylated derivatives 26 and 27, with the derivative with the alkoxy side chain at position 7 (26) being the predominant result once again. According to these findings, the hydroxyl group at C-7 is the first to be alkylated.

Only the monoalkylated derivatives 32–36 and 38–45 of 3,7-dihydroxyflavone (19) and chrysin (20) were isolated, except for the reaction of 19 with butyl iodide, which yielded the dialkylated derivative (37) as well [15].

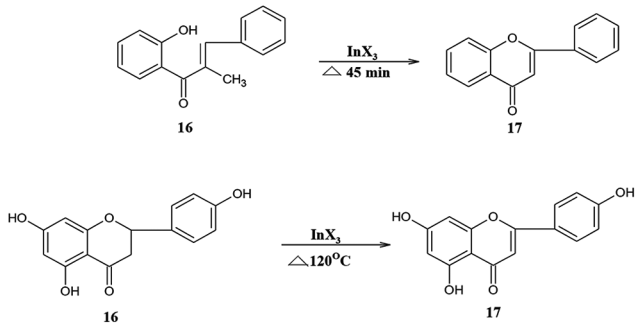
Acylation reactions

The Kostanecki acylation is an organic synthesis technique that involves acylation of O-hydroxyaryl ketones (47) with aliphatic acid anhydrides (46), to produce chromone [16] or coumarins [17], followed

by cyclization [18]. When benzoic anhydride (or benzoyl chloride) is employed, it produces a flavone (48), a form of chromone (Scheme 8).

Arylation reaction

- (a) A simple and atom-efficient palladium-catalyzed regioselective direct arylation of coumarins (49) and chromenones (50) is developed. This approach can be used to make a range of biologically relevant flavone and neoflavone backbones using a variety of electron-donating and –withdrawing substituents (Scheme 9).
- (b) Suzuki-Miyaura reactions of the bis (triflate) of 5,7-dihydroxyflavone (51) and 7,8-dihydroxyflavone (52) yielded a variety of arylated flavones (52). For electrical and steric reasons, these reactions proceed with high site selectivity in favor of ring position 7. The regioselectivity has also been investigated using DFT calculations (Scheme 10).

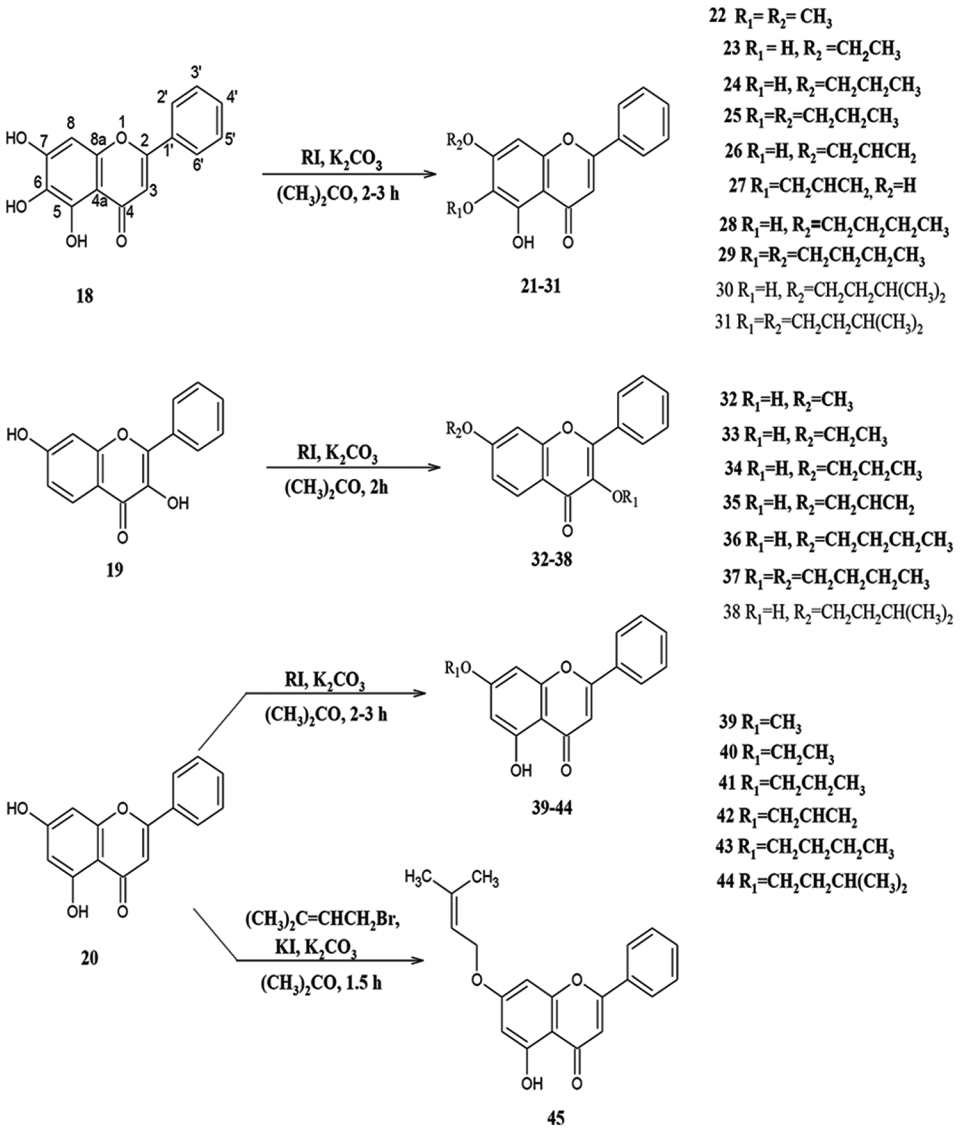


Scheme 6: Synthesis of flavones from silica gel supported InBr3 or InCl3 catalyst

Suzuki-Miyaura reactions of the bis (triflate) of 5,7- and 7,8-dihydroxyflavone occur with excellent site selectivity in favor of position 7, allowing the synthesis of a variety of arylated flavones. The reaction of 5,7-dihydroxyflavone with one equivalent of triflic anhydride also favors position 7 with excellent site selectivity. The Suzuki-Miyaura reaction permits the product to be converted into 7-aryl-5-hydroxyflavones (53). Based on DFT calculations, the regioselectivity is explored [19].

Reactions with 2'-hydroxychalcones by bromination

Bromination of chalcones (54), followed by treatment of resulting dibromides with KOH (EmilewicZ-VON Kostanecki) [20], gave the flavone-6-carboxylic acids (55) as shown in Scheme 11 [21].



Scheme 7: Synthesis of alkylation reaction of flavones

On heating 2'-hydroxychalcone dibromide (56) in alkali, flavones [22] were obtained (Scheme 12).

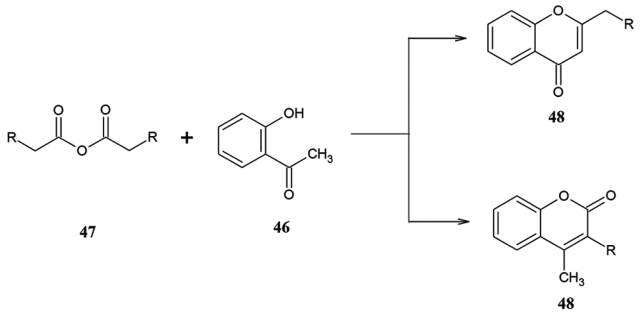
Later, Dawane [23] synthesized substituted flavone (57) by dehydrobromination followed by cyclization of dibromo-2'-hydroxychalcones in pyridine or acetic acid and potassium acetate, respectively.

Reactions with aromatic chlorine

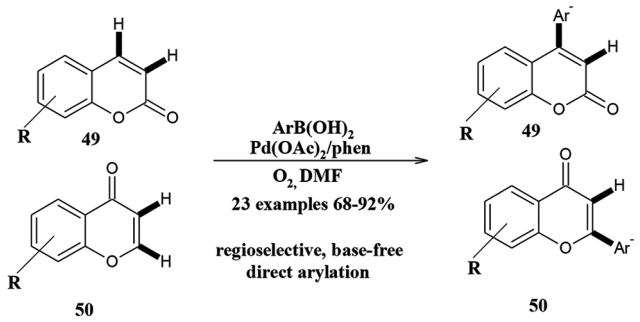
In this procedure, o-chloro phenyl benzoyl acetylene (58) was refluxed for 10 h in the presence of morpholine, yielding the flavone (59) as the final product after the morpholine hydrochloride was removed (60) (Scheme 13). The reaction mechanism is depicted as a diagram (14).

Reactions with lithium chloropalladite or palladium [II] acetate catalyzed reaction

1. Benzene was mixed with sodium methoxide and then refluxed with lithium chloropalladite or palladium [II] acetate, resulting in the synthesis of flavones at the end of the reaction [24,25].
2. Using LiHDMs and acid catalyzed cyclization reaction of *o*-hydroxyacetophenone: Reaction of *o*-hydroxyacetophenone (61) with benzoyl chloride under acidic condition using LiHDMs leads to the formation of flavones (62) in addition to the side product (63) [26]. Reaction is shown in the (Scheme 14).



Scheme 8: Acylation reaction of flavones



Scheme 9: Arylation reaction of flavones

Reactions with iodophenols and alkynes

1. From iodophenol with alkenes in the presence of pladinum catalyst: Flavones (67) were produced by reacting substituted idophenols (64) with alkynes (65) in the presence of carbon monoxide (66) and a pladinum catalyst, as reported in Daniel and Laetitia [27] (Scheme 15).
2. Iodine-aluminium trioxide (I2/Al203) microwave assisted synthesis of flavones:
   a) Substituted O-hydroxyacetophenones were microwaved with carboxaldehyde in the presence of I2-AI203/NaOH in this procedure [28]. The reaction process is depicted in (Scheme 15).
   b) From the substitution of alkene hydrogen in 4H-chromen-4-one: Flavones are produced by reducing 4H-chromen-4-one in the presence of 2,2,6,6-Tetramethylpiperidine (TMP), Zn/MgCl, and THF [29].

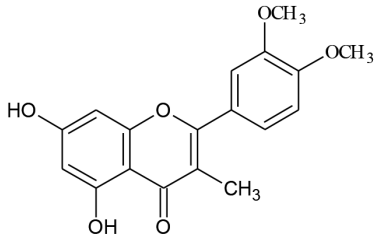
Reactions with 2'-hydroxychalcone and Potassium ferricyanide

Using potassium ferricyanide [30] in alkaline medium, an attempt was made to oxidatively cyclize 2'-hydroxychalcone to flavone. In low yields, only 2',4' dihydroxy-4-methoxychalcone (68) could be transformed into 4'-hydroxy-7-methoxy flavone (69) (Scheme 16).

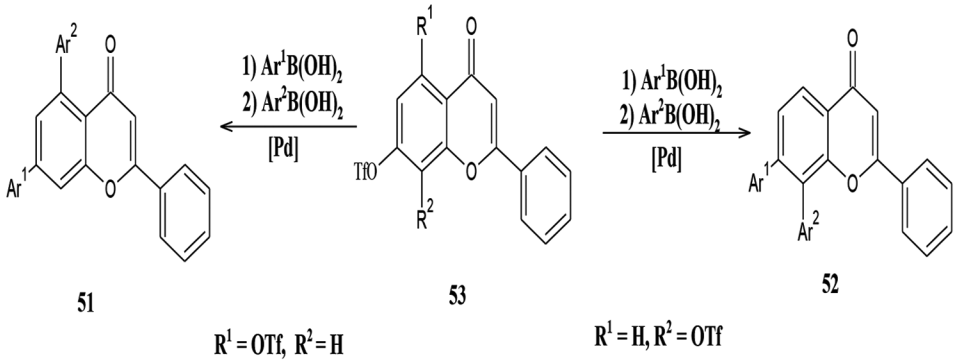
Reactions with propiophenones

In the presence of the potassium salt of 4-(benzyloxy) benzoic acid as base, 2'-hydroxy-2-methoxyacetophenones (70) were condensed with 4-(benzyloxy) benzoic acid anhydride (a). An Allan-Robinson reaction was used to make the appropriate benzyl ethers. Flavones were produced by acid hydrolysis (71) (Scheme 17) [31].

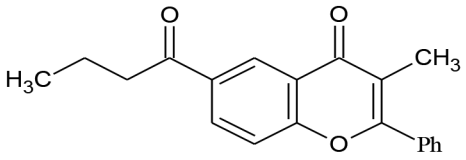
In the presence of anhydride K_2CO_3, a mixture of chloro-propiophenone and veratroyl chloride in dry acetone was refluxed for 40 h, yielding 5,7-dihydroxy-3',4'-dimethoxy-3-methyl flavone (72) [32].



6-n-Butyryl-2, 3-dimethylchromone and 6-n-butyryl-3-methyl-2-phenyl chromone (73), [33], were synthesized by treating propiophenone with acetic anhydride and sodium acetate or benzoyl chloride and sodium benzoate.



Scheme 10: Arylation reaction of flavones



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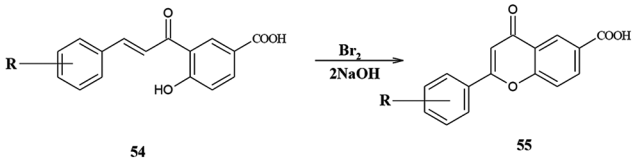
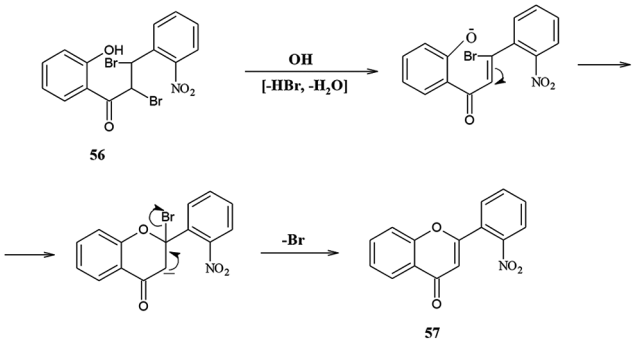
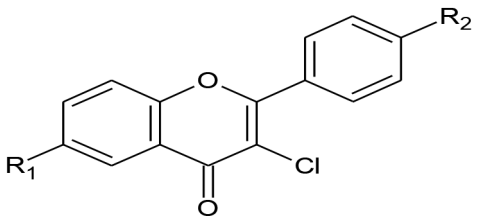


Scheme 11: Synthesis of flavones from 2'-hydroxychalcones by bromination



Scheme 12: Synthesis of flavones from 2'-hydroxychalcone dibromide

Recently, l-(2-hydroxyphenyl)-3-phenylpropan-l,3-dione in dichloromethane was agitated with ammonium chloride, hydrogen peroxide, and aqueous sulfuric acid in the presence of tetra-n-butylammonium hydrogen sulfate for 3 h to produce novel substituted 3-chloroflavones [34]. To make 3-chloroflavone, the purified and dried residue was dissolved in dry DMSO and heated with p-toluene sulfonic acid for 1 h (74).



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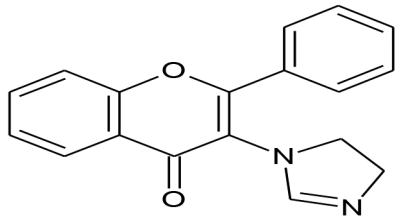
New modified 3-(lH-imidazol-l-yl) flavones (75) were synthesized in one step using a montmorillonite-KSF catalyst [35]. These compounds were also made through a well-known process, which involved pyridine condensation of some substituted acetophenone with substituted benzoylchloride.



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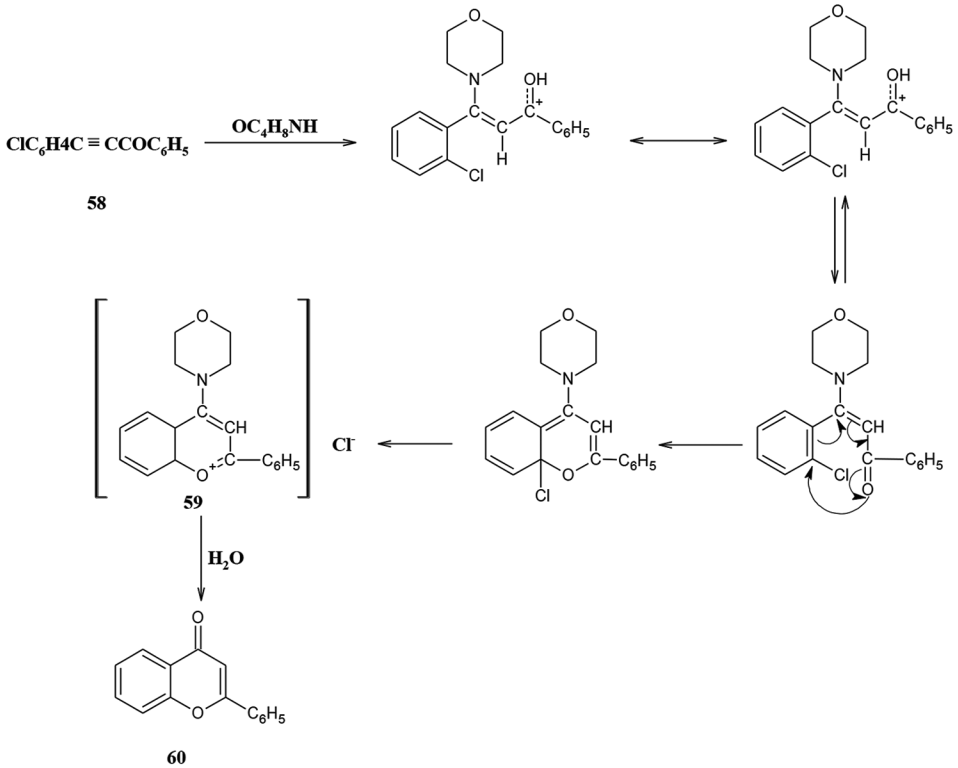
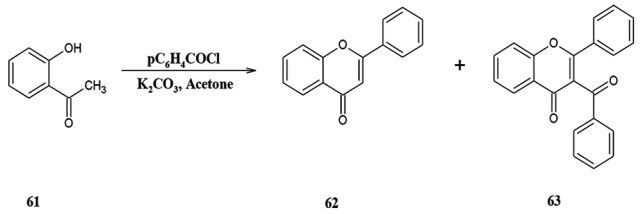
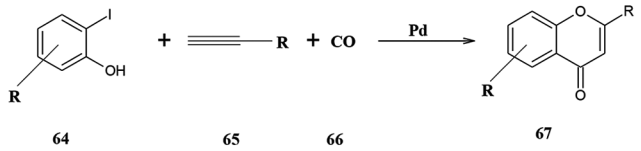


Scheme 13: Synthesis of flavones involving cyclization via displacement of aromatic chlorine

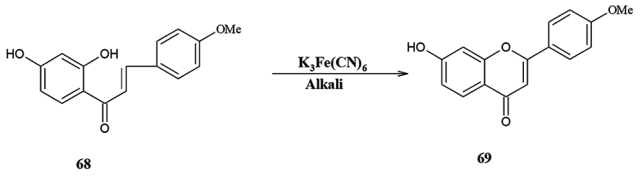
The phase transfer catalysis approach has been used to make 2-(2'-thienyl/2'-furyl) (76) and 2-o-tolyl chromones (77) (Scheme 18) [36].



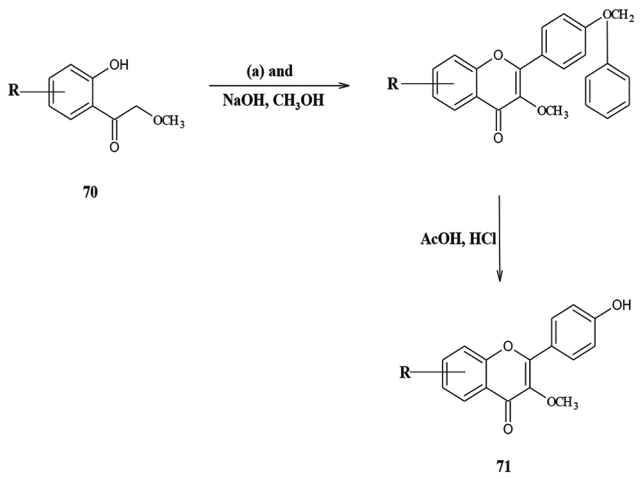
Scheme 14: Synthesis of flavones using LiHDMs acid catalyzed cyclization reaction of O-hydroxyacetophenone



Scheme 15: Synthesis of flavones from idophenols and alkynes



Scheme 16: Synthesis of flavones from 2'-hydroxychalcones and potassium ferricyanide



Scheme 17: Synthesis of flavones using propiophenones

Reactions with 2'-hydroxychalcones and iodine

2'-Hydroxychalcones were heated with dimethylsufoxide (DMSO) and a small amount of concentrated sulfuric acid at 100°C for 10 min, then a catalytic amount of iodine was added and the combination was heated at 100°C for 40 min to yield flavones. The mechanism of the response was discussed [37,38].

Doshi *et al.* [39] produced flavones from 2'-hydroxychalcones (79) by oxidative cyclization with iodine in DMSO later. Singh *et al.* [40](a) used DMSO and iodine to synthesize 2-aryl-6-[3-aryl acryloyl]-chromones (80) from matching chalcones (Scheme 19).

Lokhande *et al.* [40](b) produced flavones by refluxing chalcones with DMSO/I2 for 2 h at 130–140°C. Joshi *et al.* [41] used chalcone to make 2-(1-phenyl-3-aryl-lH-pyrazol-4-yl)-5-fluorochrome (81). The contents were cooked for 1 h at 140°C to create flavone (82). From respective o-hydroxychalcones in DMSO and a few crystals of I2, 2-benzoyl-3-methyl-7-(substituted aryl)-5H-furo [3,2-g] [1] benzopyran-5-ones [42] were synthesized (Scheme 20).

Methods for the synthesis of flavones

Flavones can currently be synthesized using a variety of methods, including the Allan-Robinson synthesis, the Baker-Venkataraman chalcone synthesis method, the Kostanecki reaction, and an intramolecular Wittig strategy.

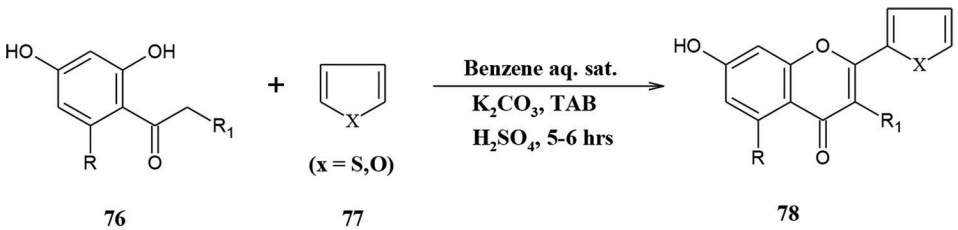
Method 1: Synthesis of flavones by Wittig reaction using phosphoranes
An intramolecular Wittig reaction is another way for the production of flavones. The triphenyl phosphonium salt is obtained by reacting acetophenone dibenzoate (83) with bromine and then triphenylphosphine (84) with sodium carbonate, followed by hydrolysis with sodium hydroxide (85) (Scheme 21) [43]. This procedure has several steps.

Method-2: Synthesis of flavones by Kalinin and co-workers [44]
Flavones and chromones (89) were synthesized through palladium catalyzed reactions of o-iodophenols (86) with terminal acetylenes (87) at 20 atmosphere pressure under carbon monoxide (88) (Scheme 22).

Method 3: Synthesis of C-C biflavones
The manufacture of two flavone analogues was used to make C-C biflavones (90) [45-47]. One was replaced with a halogen atom (bromo), while the other was replaced with groups that could be connected utilizing Pd (PPh3)4 catalysts and transition metal-catalyzed cross-coupling (Scheme 23)

Method 4: Synthesis of flavones by Baker-Venkatraman rearrangement
The Baker-Venkataraman rearrangement is a chemical process that produces 1,3-diketones by combining 2-acetoxyacetophenones (91) with a base (92) (Scheme 24) [48,49].

Enolate production is followed by acyl transfer in this rearrangement event. Wilson Baker and K. Venkatraman were the scientists that named it.



Scheme 18: Synthesis of flavones (78) using 2-(2'-thienyl/2'-furyl) and 2-o-tolyl chromones

In the synthesis of chromones and flavones, the Baker-Venkatraman rearrangement is frequently utilized [50-56]. The treatment with acid after the base-catalyzed rearrangement normally yields the flavone core chromone, while various milder approaches have been observed [57].

Method 5: Synthesis of flavones by Allan-Robinson reaction
The chemical reaction of O-hydroxyaryl ketones (93) with aromatic anhydrides to generate flavones is known as the Allan-Robinson reaction (or isoflavones) [50,58-60].

Coumarins (94) can be produced using aliphatic anhydrides (Scheme 25).

SPECTRAL PROPERTIES OF FLAVONES

1. Infra-red (IR) spectroscopy: The presence of aromatic (-C-H) stretching in flavones was shown by the IR absorption spectrum band at 3020-3070 cm^{-1}, and the presence of unsaturated carbonyl (C = 0) carbon in synthesized flavones was indicated by the absence of the –OH group band at 1600-1660 cm^{-1}.
2. Nuclear magnetic resonance (NMR) spectroscopy: The loss of the chalcone hydroxyl peak (about 13.30-13.38 ppm) [61] and relocation of the aromatic peaks were confirmed by 1H NMR spectroscopic investigation, confirming their flavone structures.
3. 13Carbon NMR spectroscopy: Due to the carbonyl group being directly linked to the oxygen atom, the carbonyl group peak shifted to a lower wave number (about 193.88-178.4 ppm), a new aromatic peak for C12 of alkene appeared, and the value of C13 shifted to a low field region. Flavone structures are so confirmed [62].
4. Mass spectroscopy: The production of flavone derivatives was also corroborated by mass spectral data. The MS principle entails ionizing chemical substances to produce charged molecules or molecule fragments, followed by mass-to-charge ratio measurements.

Scheme 19: Synthesis of flavones from 2'-hydroxychalcones and iodine

FLAVONES IN PHARMACEUTICAL AND INDUSTRIAL CHEMISTRY

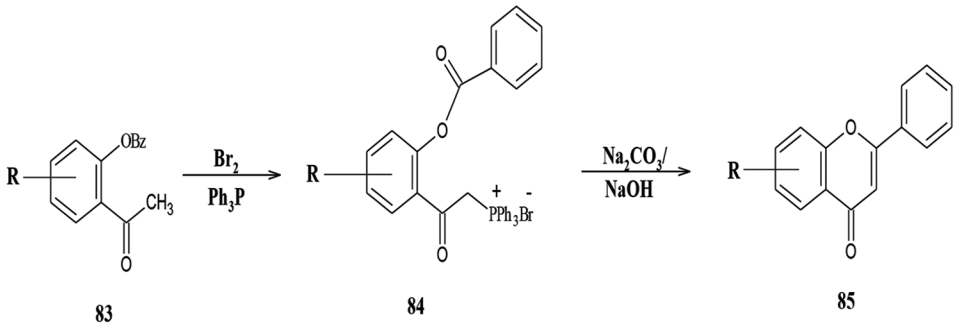
Fruits, vegetables, cereals, bark, roots, stems, flowers, tea, and wine all contain flavones, a category of natural compounds with varying phenolic structures. These natural chemicals are well-known for their health benefits, and researchers are working to extract the components known as flavones. Flavones have become an essential component in a wide range of nutraceutical, pharmacological, therapeutic, and cosmetic applications. This is due to their ability to control critical cellular enzyme activity as well as their anti-oxidative, anti-inflammatory, anti-mutagenic, and anti-carcinogenic capabilities. The discovery of a low cardiovascular death rate as well as the prevention of CHD gave flavone research a boost. The functional mechanisms of flavones are still not completely known. Plant-derived compounds, on the other hand, have long been known to have a wide range of biological activities. Flavone research and development activities are currently focused on the isolation, identification, characterization, and functions of flavones, as well as their potential health advantages. Industry is also using molecular docking and bioinformatics information to forecast potential uses and manufacture. The purpose of this study is to address current trends in flavone research and development, flavone working mechanisms, flavone functions and applications, flavone prediction as prospective medications in the prevention of chronic diseases, and future research possibilities.

Flavones are a type of natural product that belongs to a group of plant secondary metabolites with a polyphenolic structure that is commonly found in fruits, vegetables, and some beverages. They have a variety of beneficial biochemical and antioxidant properties linked to diseases such as cancer, Alzheimer's disease (AD), atherosclerosis, and others [63-65].

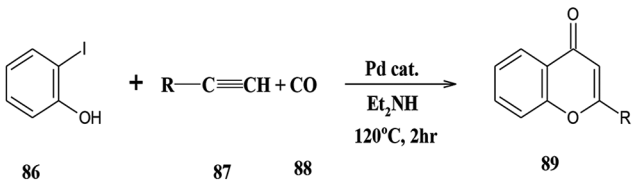
Flavones are an essential component in a variety of nutraceutical, pharmacological, medical, and cosmetic uses, because they have a wide range of health-promoting benefits. This is due to their ability to control important cellular enzyme functions as well as their antioxidative, anti-inflammatory, anti-mutagenic, and anti-carcinogenic capabilities. Several enzymes, including xanthine oxidase (XO), cyclo-oxygenase (COX), lipoxygenase, and phosphoinositide 3-kinase, are known to be powerful inhibitors [66-68].

Flavone compounds are natural chemicals taken from plants and can be found in many areas of the plant. Vegetables utilize flavones to help them grow and protect themselves against plaque [69].

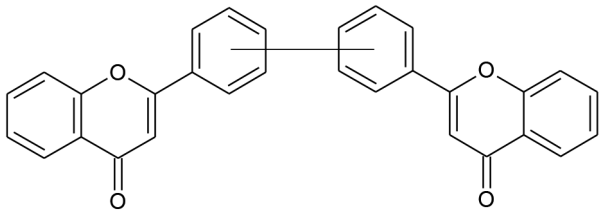
Scheme 20: Synthesis of flavones from 2'-hydroxychalcones and iodine



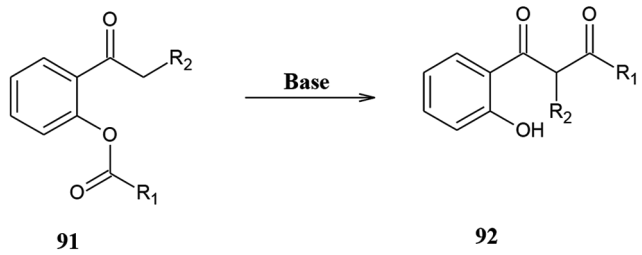
Scheme 21: Synthesis of flavones by Wittig reaction using phosphoranes



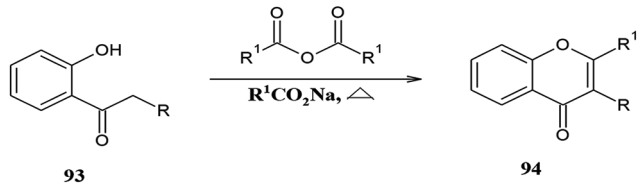
Scheme 22: Synthesis of flavones by Kalinin and co-workers



Scheme 23: Synthesis of C-C biflavones



Scheme 24: Synthesis of flavones by Baker-Venkatraman rearrangement



Scheme 25: Synthesis of flavones by Allan-Robinson reaction

They are phenolic chemicals with a low molecular weight that are found throughout the plant kingdom. They are one of the most distinctive types of chemicals found in higher plants. In most angiosperm groups, flavones are easily recognized as floral pigments. Their presence, however, is not limited to flowers; they can be found in other parts of plants [70].

Flavones have been shown to have beneficial impacts on human and animal health, and they are now being studied for disease treatment and prevention. Approximately 6000 flavones contribute to the vibrant colors seen in fruits, herbs, vegetables, and medicinal plants.

Plant flavonoids and isoflavonoids were studied in depth by Dixon and Pasinetti [71], who discussed their potential in agriculture and human neuroscience.

Flavones' protective benefits against human diseases, as well as their actions in plants, were evaluated by Kumar and Pandey [72].

Recently, Panche *et al.* [73] examined flavonoids as plant secondary metabolites for the treatment of AD and the mechanisms involved, while examining AD and current therapy strategies.

The purpose of this review is to highlight current research and development trends in flavones, as well as their uses as nutritional and health advantages, broad classification, and future research directions.

CONCLUSIONS

Flavones can be easily produced and functionalized, according to the findings. The current review has shown that flavones can be used to successfully synthesize a wide range of flavone derivatives of academic and medicinal relevance. Flavone-containing compounds have a wide range of activities. As a result, synthetic scientists and chemists have a lot of room to create new compounds with varied substitutions using substituted flavones and an appropriate heterocycle as a basic moiety. The research on this ring can still be carried out, and the flavone moiety's therapeutic value can be investigated.

AUTHORS' CONTRIBUTIONS

All the authors have contributed to the study design. The authors declare that they have no competing interests.

CONFLICTS OF INTEREST

None

FUNDING

Not applicable.

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