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Homoisoflavonoids: isolation, chemical synthesis strategies and biological activities

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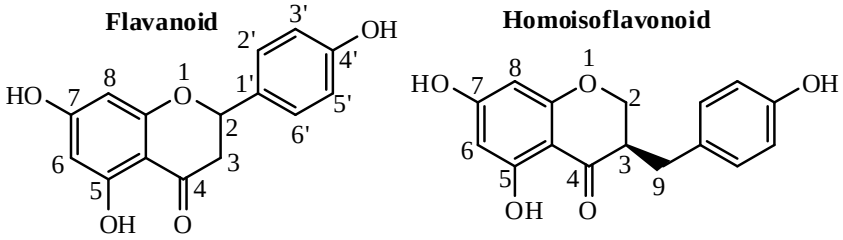
Abstract:
Homoisoflavonoids are important subcategory of flavonoids and present in wide range of plant families. Till date approximately 300 homoisoflavonoids have been identified and evaluated for various biological activities such as anti-cancer, anti-diabetics, anti-infective, anti-inflammatory anti-oxidant etc. Dominating homoisoflavonoids exhibit stereoisomerism thus isolation of a single isomer is tedious process, however, some recent advances has been made in their extraction and isolation. Moreover, the low concentration of homoisoflavonoids in plants appreciated their chemical synthesis by different methods. Homoisoflavonoids have also been explored for their molecular mechanisms which are responsible for biological activities. Here, we reviewed advancement in the isolation, synthesis and biological activities of homoisoflavonoids.

1. INTRODUCTION

The oxygen containing heterocyclics 3-benzyl-chroman-4-ones known as homoisoflavonoids (HIFs) are the phytoconstituents categorized under the flavonoids as a subcategory. The homoisoflavonoids differ from flavonoids as they have one excess carbon (C-9) which is absent in flavonoids (1). HIFs are mainly found in plants from a number of families such as *Asparagaceae, Liliaceae, Fabaceae, Convallariaceae, Hyacinthaceae, Anthericaceae, Dracaenaceae* etc. A total of approximately 300 HIFs have been obtained from roots, leaves, sapwood and heartwood of various plants till date (2). A skeleton of 15 carbon (flavonoid) acts as precursor in between the pathway of which there is addition of 1 carbons to form HIFs (3). They exhibit a vast range of biological activities as a medicinal perspective (4), (5). These biological activities includes the anti-cancer (6), anti-fungal (7), anti-viral, anti-microbial (8), anti-diabetic (9), anti-inflammatory (10), antioxidant(11) and anti-mutagenic(12). When 4-chromanones are condensed with the aromatic aldehyde using the acid/base catalyst gives HIFs which further on substitution gives the different compounds bearing different biological activity (13). Some of the HIFs are Bonducellin (*Caesalpinia pulcherrima*), Sappanone A, 2'-Methoxybonducellin and Isobonducellin (*C. pulcherrima*). In latest synthysis method Baylis–Hillman reaction is used to obtain the HIFs. The HIFs are further categorized as scillascillin-type (9), caesalpin-type (II),brazilin-type (III), protosappanin-type (IV) and sappanin-type (V) on the basis of the carbon skeletal (14).



(1) $C_{15}H_{12}O_5$ **(2)** $C_{16}H_{14}O_5$

Fig 1: The structural difference in flavonoid and HIFs (15).

2. ADVANCEMENT IN SEPARATION AND ISOLATION METHODS OF HIFS

A major problem in study of metabolites, faced is the separation, isolation and purification of the compounds. This step consumes 70% of the total efforts made during the study. New techniques of isolation, separation and purification through adsorption and high-speed counter-current chromatography. In high-speed counter-current chromatography a mixture of methanol-chloroform-water (2:4:3, v/v/v) fractionating the crude extract of 120mg at a revolution speed: 900rpm, flow rate of 1.0 mL/min. The detection wavelength was 280nm and separation temperature, 25°C. From 120 mg of an ethyl acetate extract of *Caesalpinia sappan* using this method they obtain **(4)** brazilin (18 mg), **(7)** 3′-deoxysappanol (5 mg), **(12)** 4-O-methylsappanol (20 mg) and **(9)** 3-deoxysappanone (8 mg) (16). In another advance method of high-speed counter-current chromatography for extraction of HIFs, using combination of high-speed counter-current chromatography and super critical fluid. In this method 140 mg of crude extract of *Ophiopogon japonicas* was used, out of which 98.4% pure components with different proportions were obtained. The obtained components were **(5)** 6-formyl-isoophiopogonanone A (97.3% (13.3 mg)), **(6)** 6-formyl-isoophiopogonone A (98.3% (15.3 mg)) and **(8)** methylophiopogonanone A (96.9% (4.1 mg)) (17). A centrifugation based advance method carried out to separate out and isolate the **(4)**

brazilinand **(11)** sappanol from *Caesalpinia sappan* have appeared. In this method they combined the centrifugation and chromatographic technique name partition based centrifugation chromatography (PCC) in which one step is used to separate the component and another step is use to isolate them. Solvent system used in the chromatographic step is acetonitrile:water:ethyl acetate in ratio of 1:2:1 v/v. The sample used was 350 mg for PCC which further separate out in two components **(4)** brazilin (29.6 mg) and sappanol (85.5 mg) (18).

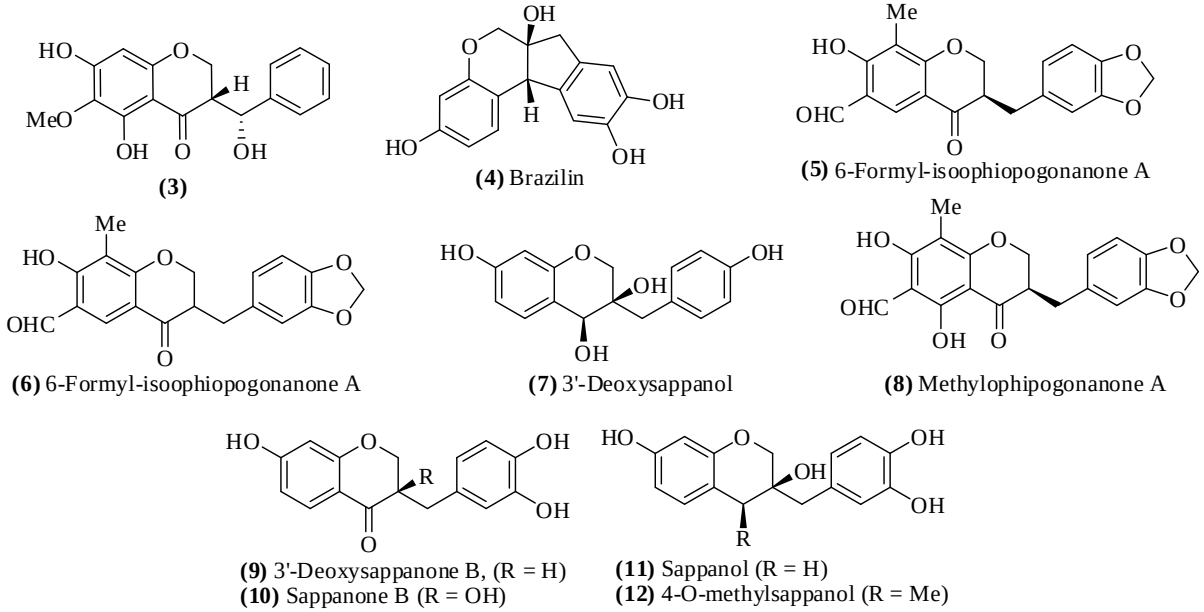


Fig 2: Different HIFs isolated and purified from different plants using advance techniques (19).

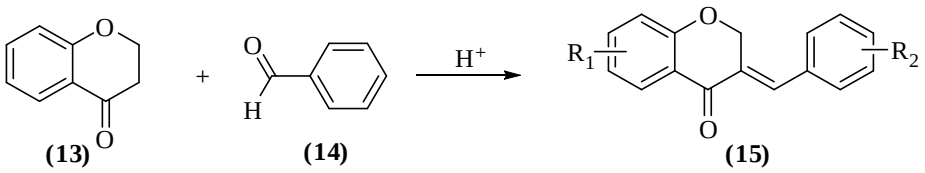


Fig 3: Synthesis of HIF using croman-4-one and aromatic aldehyde (21).

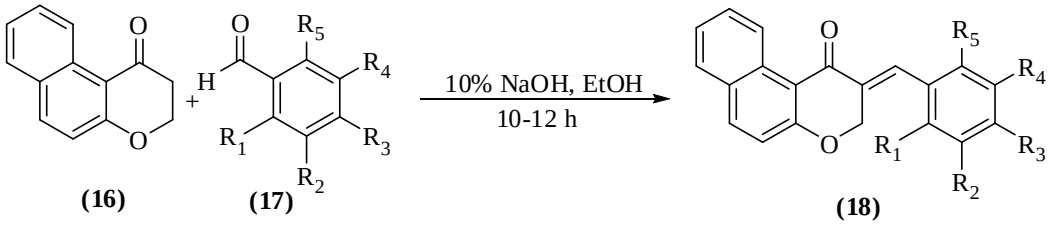
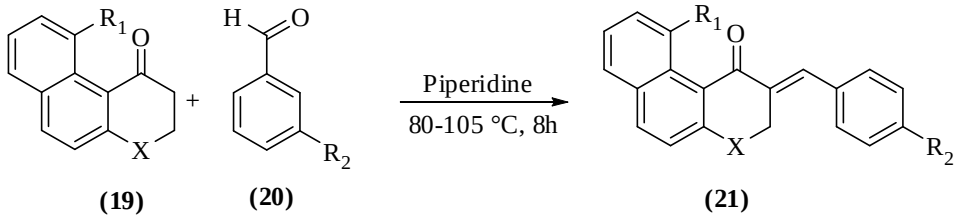


Fig 4: Synthesis of substituted HIFs using aromatic carbonyl compound.

3. STRATEGIES FOR SYNTHESIS OF HIFS

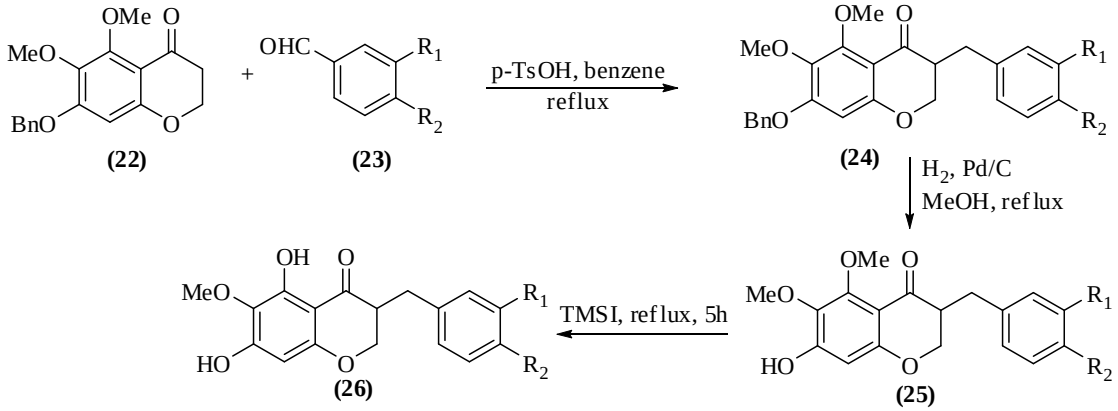
Method 1: The basic scheme to synthesize the (5)-3-benzylidenechroman-4-ones **(15)** is the condensation of aromatic aldehyde **(14)** using acid as a catalyst with the Croman-4-one **(13)**. Some of the published work has shown the same synthesis using base. But using the acid can increase the yield as well as reduces the time. This reaction has to carry out at a temperature of 60-80°C for 10-12 hour continuously (20). Some of the methods has reported the same technique using ethanol instead of acid, in which ethanol acts as the catalyst as well as the solvent.

Method 2: The second method uses the reflux reaction of benzochromanone **(16)** with the substituted aromatic aldehyde **(17)** using 10% sodium hydroxide (aqueous NaOH) in catalytic amount can lead to formation of the HIFs. In this method the NaOH is essential for the better yield. This reaction has to carry out for 10-11 hour at a temperature of 80-85°C. The aromatic aldehyde is not essential for the reaction because some of the methods reported the use of ketone (C=O) also. So any carbonyl compound can be used for preparation of substituted HIFs **(18)**. This reaction must be carried out in wide mouth flask so as to take out the precipitates from the reaction vessel. This is synthesis method is widely accepted because one can produce desired substituted HIFs by substituting the reactants (22).



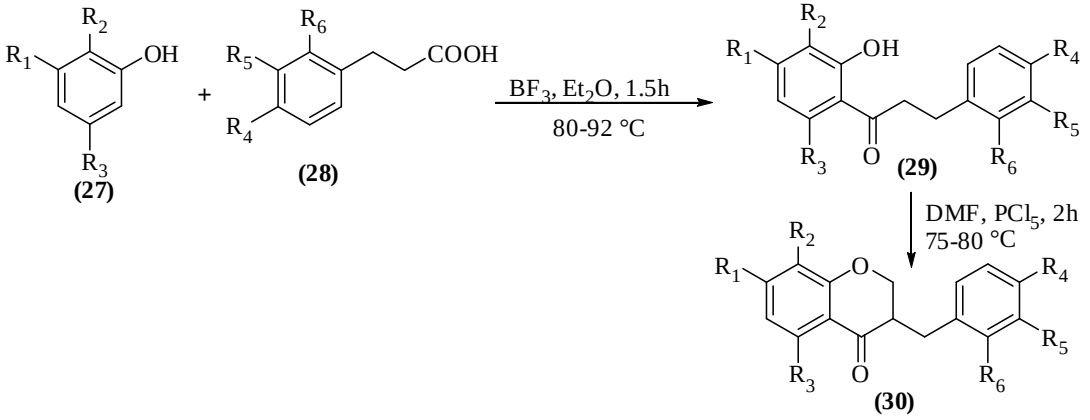
(19) **(20)** **(21)**

Fig 5: Synthesis of HIF using piperidine as a catalyst (23).



(22) **(23)** **(24)** **(25)** **(26)**

Fig 6: Multistep synthesis of 5, 7-dihydroxy-6-methoxy derivative of HIFs.



(27) **(28)** **(29)** **(30)**

Fig 7: Synthesis of HIFs using chalcone intermediates.

Method 3: This method uses the same aromatic aldehyde **(20)** and3-benzylidene chroman-4-ones (X=O**(19)**) or 3-benzylidentiochroman-4-ones (X=S) to synthesize the HIFs. In this method when an acid was used the yield decreased to 29% but using a base did not showed any increase in the yield (38%). But when instead of these piperidine was used the yield increased to 87% which is a good. So the reaction conditions included with temperature of 80-105° C and time for which reaction carried out was 8 hours.

Method 4: This method uses the 4-chromanone **(22)** was condensed with the 3,4-Disubstituted benzaldehyde **(23)** (i.e. 3,4-Dibenzyloxybenzaldehyde or vanillin). This method used the catalytic amount of acid and so as to cause demethylation at C_5 they used TMSI (Trimethylsilyl-iodide). These reactants when kept under reaction condition of 110 °C for 10 hours inside a wide mouth flask can produce 3-benzylidene-4-chromanones **(26)**. The product formation was confirmed by the spectra (1H- and 13C-NMR, mass spectrometry). Using a catalytic amount of Pd/C (3 mol %) can increase the yield by 18%. This catalyst causes the self-hydrogenation that's why the yield increases to such an extent (24).

Method 5: In this typical 2 step method of synthesis of HIFs tri-substituted phenols**(27)** and dihydrocinnamic acid**(28)** was reacted together in the presence of reagent BF_3 and Et_2O. The concentration ratio if reactants were 2:3 respectively. The reaction was carried out for 1.5 hour at a temperature range of 80-92 °C. When this first step was completed, the reaction mixture was kept for cooling (for 2 hours). After which the reaction mixture was spilled into vessel containing aqueous sodium acetate. Then this mixture was treated with ethyl acetate as a result of which Dihydrochalcones**(29)** were produced. In 2^{nd} step of this reaction Dihydrochalcones were reacted with N,N-dimethyl(chloromethylene)ammonium chloride (25), using DMF as a solvent system and PCl_5 as a reagent which gives a carbon extension required for the formation of HIFs. Completion of this step requires appropriate temperature range of 75-80 °C for 2 hours continuously.

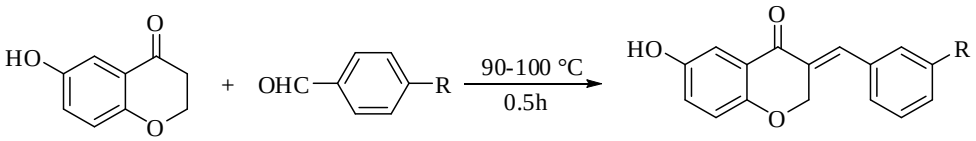
As a result of all this substituted HIFs**(30)**can be obtained at the end of reaction. Whole reaction was monitored using TLC and confirmation of product was done by using NMR and mas spectra. The substitution at different positions of the resultant HIF causes the variation in the product yield which is given in **Table 1** (26).

Table 1: The effect of substitution on the yield of HIFs **30a-h**.

Sr. No.	R_1	R_2	R_3	R_4	R_5	R_6	% Yield of HIFs
30a	OH	H	H	OH	H	H	85
30b	OH	H	H	OCH_3	H	H	88
30c	OH	H	H	OH	OH	H	82
30d	OH	H	H	OCH_3	OCH_3	H	87
30e	OH	H	H	OCH_3	H	OCH_3	78
30f	OH	OH	H	OH	H	H	80
30g	OH	OH	H	OCH_3	H	H	81
30h	OH	H	OH	OH	H	H	85

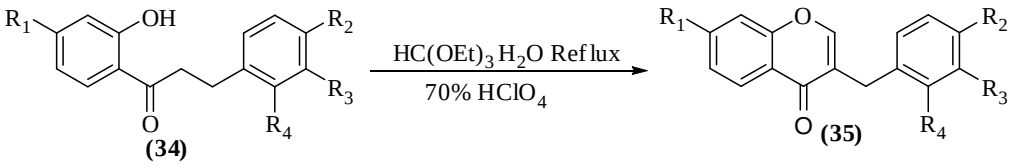
Method 6: This method is typically solvent free. In this method solvent less reaction is carried out between the **(31)**chroman-4-onesderivative with the **(32)** *p*-chlorobenzaldehyde(27). This reaction is very eco-friendly and less expensive as this reaction do not uses the solvent and takes only 30 minutes to complete. The reaction conditions requires is 90 °C and constant stirring. After completion of reaction the product was separated and purified through silica gel. Another method with same reactants suggests the use of *p*-methoxybenzaldehyde(28). As the use of this reactant instead of chloro derivative increases the product yield by 12% and formation of by-products is also less in this. The whole reaction was monitored through TLC and product formation was confirmed by using mass spectrometer (29).

Method 7: This is a novel method of synthesis of the HIFs which involves the reaction of 2'-hydroxydihydrochalcones**(34)** using triethylorthoformate ($HC(OEt)_3$) in a medium of 68% of perchloric acid which provides an acidic media as well as the source of $H^{+,}$ required for the activation of reactants and for aqueous hydrolysis. This all gives an unsubstituted novel HIF**(35)** which can be further substituted according to the activity required. But another literature available on the same method has reported that using a 70 % of perchloric acid media gives more yield of the resultant HIF. It further added that use of perchlorates has improved the yield which as a result becomes 87%. The whole reaction was monitored through the TLC and confirmation of the product formation was done through determination of physicochemical properties.The substitutions at the reactant sites has variations accordingly which has its effect on the yield of final product which is shown in **Table 2**. The resultant HIFs had several activity such as anti-fungal, anti-diabetic and anti-oxidant(30).



(31) **(32)** R= Cl, OCH_3 **(33)**

Fig 8: Catalyst and solvent free synthesis of HIFs using chroman-4-ones derivative.



(34) **(35)**

Fig 9: Perchloric acid catalysed synthesis of HIFs from hydroxydihydrochalcones.

Table 2: The effect of substitution on yield of HIFs (**35**).

Sr. No.	R_1	R_2	R_3	R_4	% age yield of HIF
35a	H	H	H	H	65
35b	OCH_3	OBz	OCH_3	H	68
35c	OCH_3	OCH_3	H	OCH_3	82
35d	Cl	Cl	Cl	Cl	75
35e	H	H	H	H	87
35f	OBz	OCH_3	H	H	67
35g	OCH_3	H	H	H	82
35h	H	OBz	OCH_3	OCH_3	81
35i	H	OCH_3	OCH_3	Cl	79

Method 8: This reaction consists of combination 3 steps or 3 different reactions named hetero Diels-Alder reaction, Diels-Alder's addition and CH-alkylation. In this reaction condensation between *ortho*-(N,N-dimethylaminomethyl)phenol **(36)** and (2E)-3-(N,N-dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-ones **(37)** in which the first step is CH alkylation using BnBr, and DMF as a solvent which leads to formation of an unstable intermediate **(38)** after which the cascade addition reaction occurs which further changes to Diels alder's reaction and finaly the HIF formation occurs. The total yield observed was 87% and confirmation was done through the mass spectra (31).

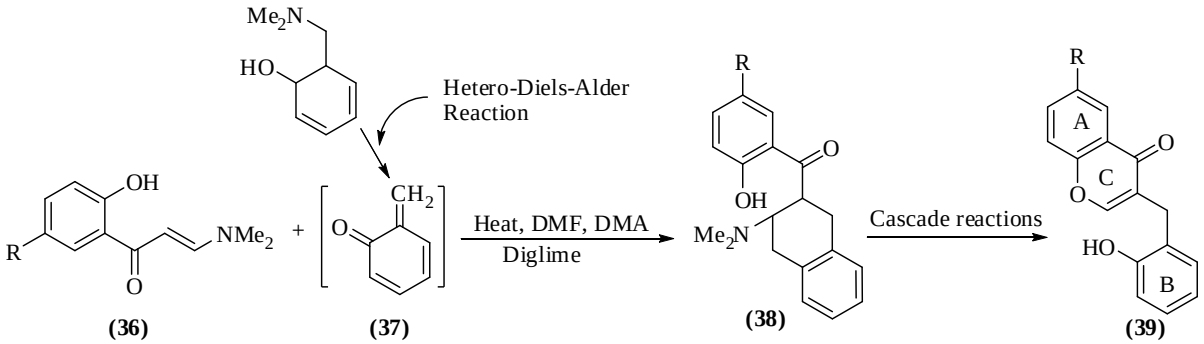


Fig 10: Synthesis of HIF (39) via Hetero Diels-Alder reaction.

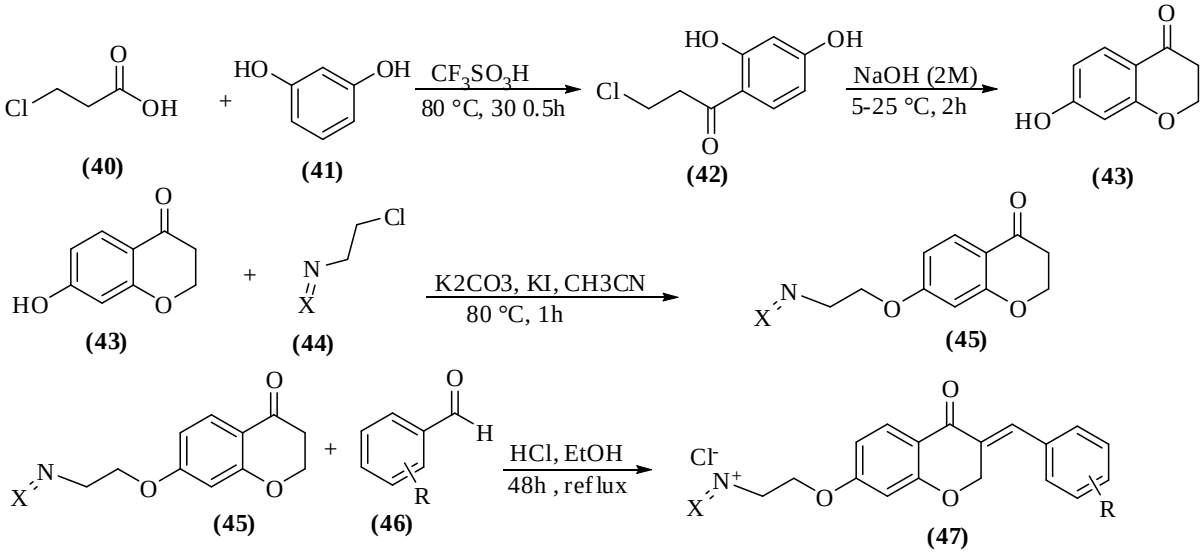


Fig 11: Multistep Synthesis of 7-amino alkoxy homoisoflavonoids (**47**).

Method 8: This method is a short form yet an old method of synthesis of the HIFs. Most of the reactions used 4-chromanones as a starting material but this reaction is so basic that it has 3-4 steps of reactions starting from very basic reactants which lead to formation of 4-chromanones in between reaction. In this reaction condensation of the 3-chloropropionic acid **(40)** and resorcinol **(41)** occurs as a first step which leads to formation of 2,4-dihydroxy-3-chloropropiophenone **(42)**. The reaction conditions required are CF_3SO_3H in catalytic amount and the reaction has to carry out for 30 minutes at a temperature of 80 °C. Then in second step 2,4-dihydroxy-3-chloropropiophenone **(42)** is treated with 2M solution of NaOH and the temperature should be maintained in a range of 5-25 °C. The resultant of second step was 7-hydroxychroman-4-one **(43)** through cyclization of 2,4-dihydroxy-3-chloropropiophenone. Then in third step the 7-hydroxychroman-4-one was reacted with aminoethylchlorides**(44)** in the presence of K_2CO_3,CH_3CN and KI at a temperature of 80 °C for 1 hour which leads to formation of 7-aminoalkoxychroman-4-ones **(45)**.

The total yield observed was 70-76%. The activation of the aminoethylchlorides was done using KI. In next step the 7-aminoalkoxychroman-4-ones with substituted aryl aldehyde **(46)** using acidic medium and EtOH leads to formation of novel HIF**(47)**. The last step was carried out at a temperature range of 80-85 °C and refluxed for 48 hours. The total yield observed was 56-60%(32).

Method 9: This is somehow different than others because this method uses vilsmeier reagent(33) for the synthesis of the chromanones moiety then further normal HIF synthesis is carried out. This is two step reaction in which first step is to prepare the vilsmeier reagent using classical method then second step is to synthesize the chromanones moiety. In this firstly the 1,4-dioxane**(50)** is treated with phthaloyl chloride**(49)** using dimethylformamide **(48)**(34) as a solvent at a temperature of 40 °C for 3 hours. The obtained precipitates will consist of vilsmeier reagent**(51)** and phthalic anhydride. The reagent was separated out using various separation methods. The product formation was confirmed using the TLC. In the second step 2-hydroxyacetophenone**(52)** was treated with the vilsmeier reagent. The 2-hydroxyacetophenone was activated using Et_2O and BF_3 was used as a catalyst. The reaction conditions implemented was a temperature range of 40-50 °C and reaction was carried out for 30 minutes which results in chromanones moiety **(53)**. Then further it was treated with *p*-chlorobenzaldehyde**(54)**which gave the desired HIF**(55)**. The resultant product was confirmed using mass spectrometer and whole reaction was monitored using TLC(35).

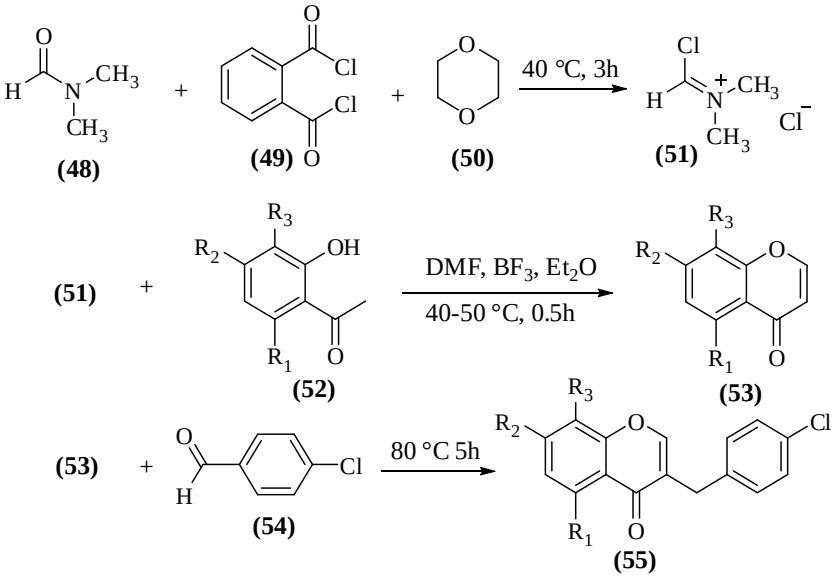


Fig 12: Multistep synthesis of HIFs (**55**) using the Vilsmeier reagent.

4. BIOLOGICAL ACTIVITIES OF HIFS

There are various medicinal applications of the natural products. In starting of era a few synthetic compounds were there which are active against some pathogens or microorganisms(36) even some of them were semi-synthetic but a variety of the natural compounds were there which saved a number of people in that era(37). In this modern era the main drawback of each synthetic compound there is an adverse effect of each(38). Some of the synthetic compounds have even more adverse effects than its biological activity. So choosing natural products over synthetic was always a choice(39). HIFs are naturally occurring a subclass of flavonoids which has medicinal importance because of various medicinal applications of it (40). This class has a range of compounds required for use in daily lifestyle to the compounds required to treat life threatening diseases like cancer and diabetes (41). Current research on HIFs is oriented towards the metabolite study as well as the new drug application of the HIFs. This all medicinal importance and other characters are making this sub-class of flavonoids a bit more special than others (42). This class has different compounds which are distributed over different parts of different plants. Each part of these plants has specific medicinal importance. Such as the bulb of some plants of this class has anti-hypertensive activity. The total extract of some plants are used as anti-inflammatory agent. Flower petals of some plants of this class has blood circulation improving property (43) like this HIFs have various medicinal importance, out of which few are as follow:

4.1 Antioxidant

HIFs are tremendous antioxidants along with free radical scavenger activity. Various compounds such as bonducellin**(56)**, isobonducellin**(57),**2′-methoxy-bonducellin **(58)**, Sappanone A**(59)**, eucomin **(60)** and 8′-methoxy-bonducellin **(61)** possess a strong antioxidant activity. Some of other publications reported their activity similar to the vitamin C, butylated hydroxyanisole (BHA) and butylatedhydroxytoluene (BHT) (44). Their antioxidant ability was tested using a test solution in which methanol and ethanol was mixed along with sample. The reference solution was methanolic mixture of 2,2-diphenyl-1-picrylhydrazyl (DPPH)-a compound that is composed of a stable free radicals. The percentage inhibitory value was calculated using UV-spectrophotometry, in which comparing the absorbance value at specific wavelength of 512nm of both. The 50% inhibitory concentration of these compounds were observed. Most of the compounds were having similar inhibitory concentration also their free radical scavenging ability was checked against DPPH. In this test the scavenging activity of the HIFs were sufficient to cause antioxidant activity (45). The HIFs were found to be active against the 5-lipoxygenase at an IC_{50} of 10µM. Their antioxidant activity was also checked on biological system having some enzymatic action. In this enzymatic induced peroxidation of the lipids were compared against the inhibitory action of vitamin E and BHT(46).

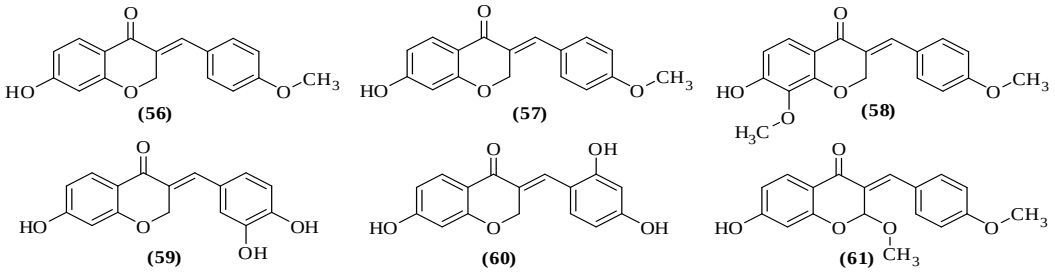


Fig 13: Represents the compounds having antioxidant activity.

4.2 Anti-fungal

Various HIFs such as brazilin **(4)**, 4-O-Methylsappanol **(62)**, caeasalpin **(63)** and protosappanin A **(64)** have been reported for their anti-fungal activity. Reddy *et al* isolated above mentioned compounds by extracting it from plant *Caesalpinia sappan.* They have checked the inhibitory action of these compounds using a culture of fungi *Beauveria bassiana.* They have used modified liquor media prepared by agar-well method. In this test 4-O-Methylsappanol showed a great inhibitory activity at a concentration of 100 µg, while other compounds of the series showed a good activity at a concentration range of 100-140 µg. So all this evidences showed that the HIFs possesses the anti-fungal activity (47). Moreover HIFs as anti-fungal do not have any adverse effects, which could be a major advantage over synthetic anti-fungal drugs (48). Madhava *et al* also reported the same antifungal compounds and their derivatives. They used petri plate method to determine the anti-fungal activity. They firstly sterilized all the glassware to be used in the process. They used dextrose (4g) and peptone (1g) in 100 ml of distilled water, previously warmed. In this process medium was prepared using agar with peptone and dextrose which was saboroudes agar medium. They inoculated the culture and kept this for incubation overnight. The temperature was maintained at 25 °C. Then next day the compounds to be tested were put on the same petri plates in a volume range of 10-20 µL. After a week the plates were collected and inhibitory zones were measured to check the compound activity. This leads to a result that 4-O-Methylsappanol and brazilin were having a effective area of inhibitory, while other compounds were showing a satisfactory result (49).

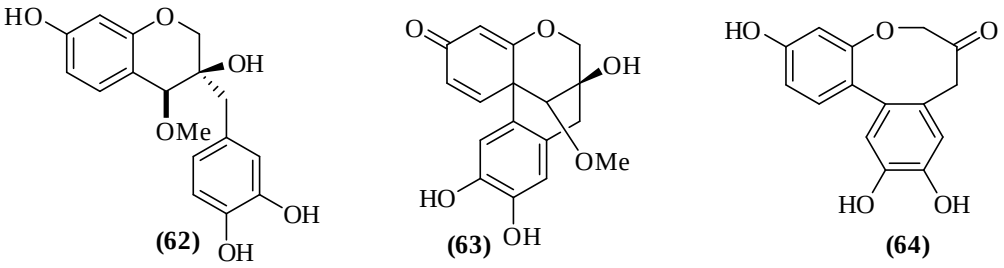


Fig 14: Chemical structures of the anti-fungal homoisoflavanoids.

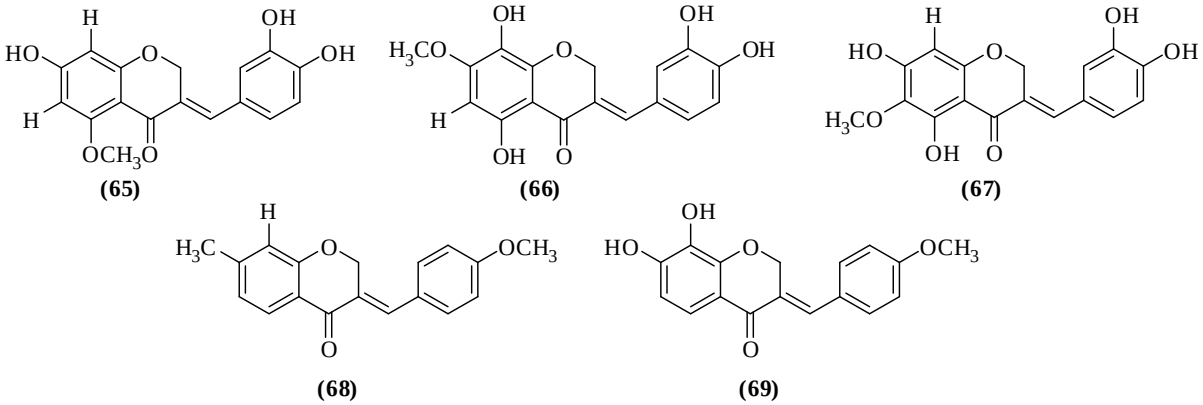


Fig 15: Structurs of anti-mutagenic homoisoflavanoids obtained from *Hoffmanosseggia intricate* and *Muscari racemosum.*

4.3 Anti-mutagenic

In a study, Wall *et al.* have been reported the anti-mutagenic activity of some compounds of homoisoflavanoids. Compounds such as intricatinol**(69)** and intricatin**(68)** showed anti-mutagenic activity which were isolated from the plant *Hoffmanosseggia intricate.* They have evaluated the anti-mutagenic activity against the ethyl methane sulfonate (EMS), acetylaminofluorene (AAF) and 2-aminoanthracene (2AN) as standard using strains of *Salmonella typhimurium.* Further it was found that intricatin is more active that EMS and their methyl analogues were having less activity than the hydroxyl derivatives (50). Masterova *et al* has reported that ethanolic extract of *Muscari racemosum* containing high concentration of HIFs has anti-mutagenic activity. They reported the compounds having anti-mutagenic activity were the derivatives of benzylidene-4-chromanones**(65, 66 & 67)**. They all were evaluated using the strains of *Salmonella typhimurium* all the compounds were showing great effects. So by all this, it is concluded that HIFs are also having anti-mutagenic activity (51).

4.4 Anti-diabetic

Some publications has reported to have anti-diabetic activity of the HIFs(52). Most abundant compounds such as isobonducellin **(57)** and 2′-methoxy-bonducellin **(58)** derivatives are said to be have *α*-Glucosidase inhibitory action which was evaluated for activity using acarbose as a reference. In this assay Miyazawa *et al* has used 50 mM phosphate buffer having pH of 6.8 in which 30 µL of 0.25

U/mL α-glucosidase along with 100 mM NaCl was dissolve and prepared a solution. A substrate (30 µL of 7 mM PNP-G) was also dissolved in the buffer. A usable volume of 210 µL of above prepared solution was taken and dissolved in DMSO (dimethyl sulfoxide) so as to prepare a number of samples to be assayed. Then these samples were evaluated using the Molecular Devices which was SPECTRA MAX 190. A positive response was seen at an absorption maxima of 405 nM with respect to the acarbose (53).

4.5 Anti-inflammatory

Anti-inflammatory activity of the HIFs are important factor due to which HIF have a special space in the medicinally important natural products. Some plants having HIF such as *Caesalpinia sappan* found to have some anti-inflammatory and analgesic properties(54). Oh *et al*has reported that brazilein**(70)**, brazilin**(4)**, protosappanin E**(71)**and protosappanin B **(72)**has anti-inflammatory and analgesic activity. Their activity has been evaluated using NO as efficiency of inhibiting the nitric oxide synthase (iNOS). In this all three compounds showed a great desirable activity. They were also evaluated against lipopolysaccharide (LPS)-stimulated NO formation, in which brazilin was efficient to inhibit the formation of NO. Other compounds were able to inhibit the LPS-induced iNOS protein in a specific dose pattern. These compounds were activating the macrophages to act as first line of defence(55).

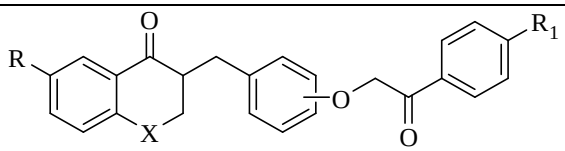
4.6 Anticancer

Demirayak *et al.* has reported that chroman-4-one/thiochroman-4-one derivatives **(73-107)** are consisted with potent anti-tumour activity (Table-3). They evaluated the anti-tumour activity against various cell lines of human breast and liver cancer. Among, 34 compounds were found to have good activity but thiochromanone skeleton was most efficient and powerful anticancer agent (56).

4.7 Anti-microbial

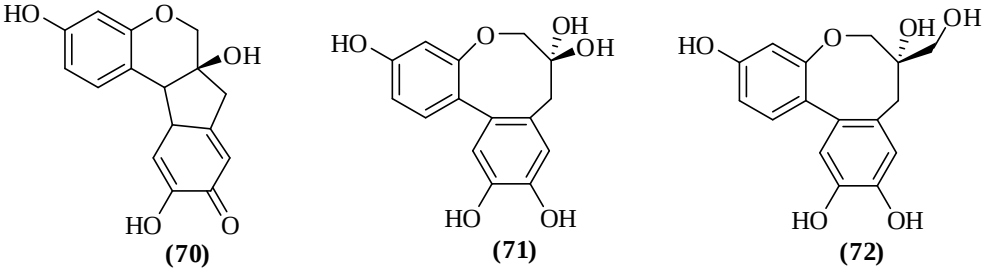
Homoisoflavanoids have also been possessed the anti-microbial activity. Chloroform extract of some plants such as *Dracaena loureiri* which is an important medicinal plant of Thailand possess anti-microbial activity. This extract consist of various rare types of homoisoflavanoids which were evaluated against *Escheria coli, Bacillus subtilis*, and *Staphylococcus aureus* and all the compounds showed desired inhibition at a concentration of >25 µL. Other compounds such as bonducellin **(56)** and isobonducellin **(57)** were found to be a broad-spectrum inhibitors (57).

Table 3: HIF derivatives (**73-107**) with diverse substituents.



(73-107)

Compound	R	R_1	X
73	H	H	O
74	H	CH_3	O
75	H	OCH_3	O
76	H	Cl	O
77	H	H	O
78	H	CH_3	O
79	H	OCH_3	O
80	H	Cl	O
81	Cl	H	O
82	Cl	OCH_3	O
83	Cl	Cl	O
84	Cl	OCH_3	O
85	Cl	Cl	O
86	Cl	CH_3	O
87	H	H	O
88	H	H	S
89	H	Cl	S
90	H	CH_3	S
91	H	OCH_3	S
92	H	OCH_3	S
93	H	Cl	S
94	H	Cl	S
95	CH_3	H	S
96	CH_3	H	S
97	CH_3	CH_3	S
98	CH_3	OCH_3	S
99	CH_3	Cl	S
100	CH_3	H	S
101	Cl	CH_3	S
102	Cl	OCH_3	S
103	Cl	Cl	S
104	Cl	CH_3	S
105	Cl	CH_3	S
106	Cl	OCH_3	S
107	Cl	Cl	S



(70) **(71)** **(72)**

Fig 16: Structures of HIFs with anti-inflammatory activity.

CONCLUSION

Homoisoflavonoids are found in numerous plant families and known for their diverse biological activities. The progress in chemistry of homoisoflavonoids has been made as development of different methods for chemical synthesis of these compounds. Till date approximately 300 homoisoflavonoids have been identified with different biological activities. The provided synthetic methods, mechanism based biological activities and potencies of different homoisoflavonoids will help to improve their synthesis and target specific activities.

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Conflict of interest

Authors declare no conflict of interest.

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