2022
9(4), 374

Chemical Biology
LETTERS

Medicinal active applications of Dibenzofuran derivatives

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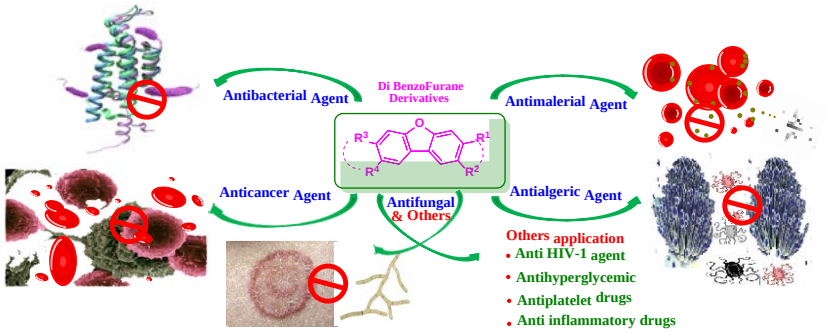
Submitted on: 25-May-2022, Accepted and Published on: 02-July-2022

Review

ABSTRACT



Dibenzofuran is an important heterocyclic compound and is an important part of various natural compounds. There are various medicinal compounds containing dibenzofurans, sold in the market to combat different human diseases and plant infections. Research on dibenzofuran is an advancing field in the medicinal science. Several compounds are under the clinical trials and are expected to be utilized in various treatments. This review article encompasses various advancements in the study of these dibenzo derivatives. The biological activity of these scaffolds hovering around cytotoxicity of the cells, bacterial infections, fungal infections, type-2 diabetes, platelet coagulation and in the effective skin treatment, has been discussed in the following article. The toxicology of the compound is also argued and selected biological applications are hereby discussed to make easier for the researchers to have a consolidated sight over the topic.

Keywords: Dibenzofuran Derivatives, Antibacterial Activities, Anti-cancer, Anti-malarial, Anti-fungal, Hyperglycemia, HIV-AIDS

INTRODUCTION

Dibenzofurans are heterotricyclic organic complexes with furan ring ortho-fused across 2,3- and 4,5- positions of the two benzene rings. The potent environmental pollutant mostly found in groundwater,[1] air[2] and also in the cigarette ash[3] turns out to be widely used in the pharmaceutical industry on the other hand. The exploitation of this compound lets the scientists to develop several biologically active compounds with varied application in the medicinal chemistry. Most of the dibenzofurans and their derivatives can be isolated and extracted from the wide variety of natural sources ranging from slime molds to large trees.[4–7] Whereas many scientists have putforth different synthetic methods ranging from the intermolecular C-C bonding and intramolecular C-O bond formation.[8–11] Cu-catalyzed deborylative ring contraction of dibenzoxaborins by Sumida *et.al*,[12] Visible-light induced aromatization of 2-Vinyloxy arylalkynes by Chen and co-workers.[13]

Because of the varied chemical and biological properties, dibenzofurans are employed as the important complexes in variety of natural products[14,15] and synthetic materials. Dbfs' uses have covered a vast field owing also to its weak biochemical stress response and high heat resistance.[16,17] They provide strong backbone for the formation of decorated coordination compounds due to its rigidity.[18] Whether in molecular probes[19] or in the photochemistry for the production electrophosphorescent organic light emitting diodes,[20] Dbfs and their derivatives have participated vigorously across the time.

Dibenzofurans as the phytotoxins, anti-cancer agents and anti-bacterial agents have surpassed many pharmaceutical industry favourites. Therefore, the biological properties of such a compound should be even more altered to gain utmost advantages from such a privileged motif. This review encompasses several such advances happened down the line in the segments; anti-cancer, phytotoxic, anti-bacterial, anti-fungal and as anti-HIV agents,[21,22] Cytotoxic[23,24] and Antiplatelet Activities,[25] cotonefurans[26] in the medicinal chemistry, which gives an easy access of the proper knowledge to the researchers, to develop not only more bio-active compounds with increased biological activity but also varied applicable complexes.

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URN:NBN:sciencein.cbl.2022.v9.374

ISSN: 2347–9825
https://pubs.thesciencein.org/cbl

Biological Activity

The derivatives of dibenzofurans are widely used in medicinal chemistry. They show a lot of biological activities like anti-cancer activity, anti-bacterial, anti-fungal activity, anti-malarial, anti-allergic, anti-HIV-1 agent, anti-hyperglycemic, anti-platelet, anti-inflammatory.

stop the growth of cancer cells. The said dibenzo derivative proved to have efficient inhibiting ability at a relatively low concentration (IC50 = 400 nm). To add on its advantages, the authors also confirmed that it is not cytotoxic to CV-1 nontumor monkey kidney, whereas potentially cytotoxic (IC50 =2.5 µg/ml) to A549 non-small cell lung cancer cells. There has been many ongoing research carried out on this dibenzo derivative **1** owing

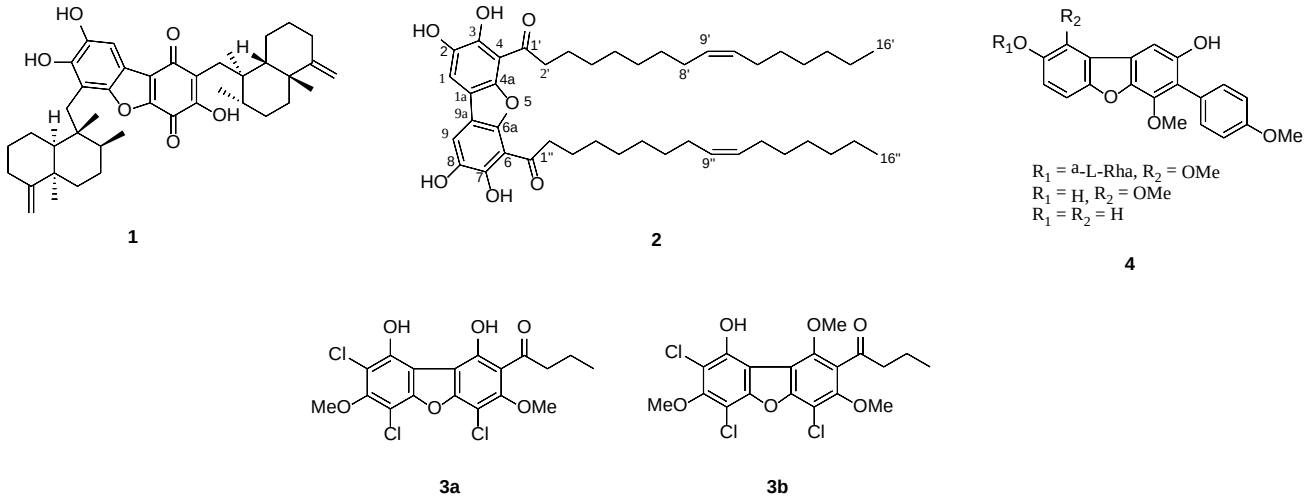


Figure 1. Biological active dibenzo furan containing anticancer agents.

Anticancer Activity

The notorious fatal disease characterized by the development of uncontrobally divisible abnormal cells, can easily destroy the normal body tissue. The most common disease of 2020 as per the WHO reports, is responsible for about 10 million deaths per annum. Right from the beginning, the search for more and more efficient methods, therapies and the drugs is being carried out to save millions of lives. Chemotherapy, gene therapy and protein therapeutics are some of the popular ones adapted.[27,28] Every other research tends to improve the therapy and curb the difficulties of the people. Some dibenzo furan derivatives have proved to be cytotoxic, which even can be synthesized in simple processes. So, we hope that the further research on these complexes can led to some astonishing results.

Popolohuanone (E) **1** an oxidatively-dimerized arenarol derivative was isolated from the freeze-dried Dysidea sponge, collected at Pohnpei in the year 1993[6]. This was a breakthrough in the field of inhibitors of Topoisomerase-II; a target enzyme for most of the effective anti-cancer agents. T-II supports the DNA replication, which must be inhibited by the anti-cancer agents to

to its capability matching the currently usable anticancer agents for lung cancer like epipodophyllotoxins.

The Scyphocephalium ochocoa is a medicinal tree belonging to western African tropical region. Tchouya and his co-workers revealed the presence of a dibenzofuran, within this plant which could be reason for its medicinal activity in the year 2021.[29] They extracted the yellow powdered form of the dibenzofuran and characterised it by using several techniques like IR, UV, MS, 1 D- and 2-D NMR. From the investigations, they proved that the new dibenzofuran derivative **2** found in the stem bark of the plant has potential medicinal capability and also has anti-inflammatory behaviour. Thus, it could be used as an efficient chemotherapeutic agent.

Cellular slime molds were again used for the production of the secondary metabolites including polyketides. This time the fruiting bodies of Dictyostelium discoideum was utilized for the production of chlorinated dibenzofurans Pf-1 **3a** and Pf-2 **3b**.[5] The compounds share similar structural formula with AB0022A,[30] thus all three were tested for their effects on cell growth in K562 leukemia cells, HeLa cervical carcinoma cells and mouse embryo fibroblast 3T3-L1 cells. To the better, the

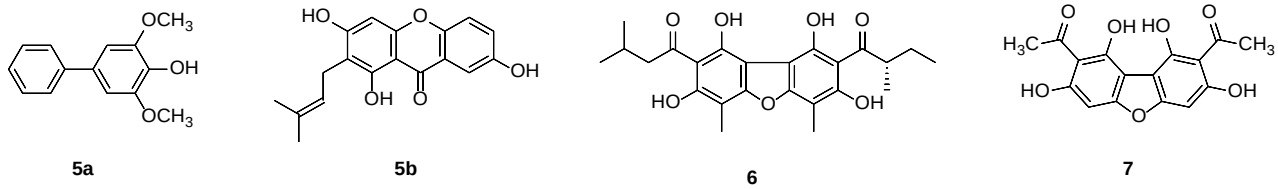
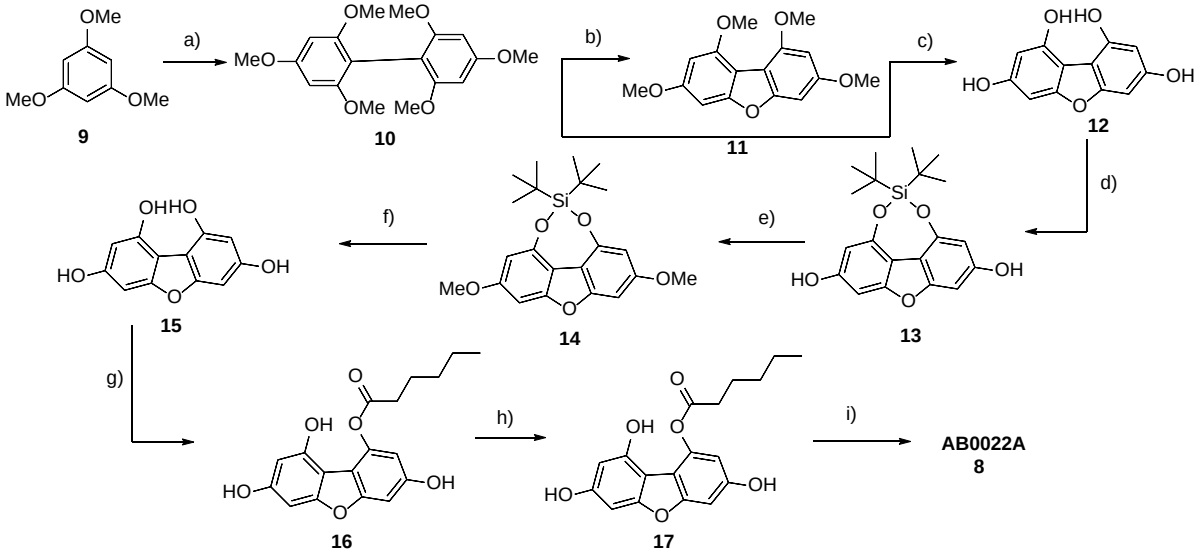


Figure 2. Biological active dibenzo furan containing anticancer agents.

authors reported significant cell growth suppression by Pf-2 and AB0022A and also credited it to the presence of the free phenolic group adjacent to the carbonyl carbon.

make efficient drugs that also are less probable to undergo the resistance.

In the year 2002, Cortez and his co-workers reported their



a) i) HIO_3, I_2, EtOH, reflux, 30 min, 91%, ii)Cu, 240 °C, 6h, 81%; b) 57% HIaq. reflux, 30 min, then CH_3I, K_2CO_3, DMF, r.t., 3h, 12%(lit 37%[3]); c) 57% HI aq., AcOH, reflux, 15h, 84%; d) (tert-Butyl)$_2$Si(OTf)$_2$, 2,6-lutidine, DMF, 0 °C, 30 min, 67%; e) CH_3I, K_2CO_3, DMF, r.t., 4h, 97%; f) tetra-n-butylammonium fluoride, THF, r.t., 30 min, 94%; g) caproyl chloride, pyridine, CH_2Cl_2, 0 °C, 30 min, 66%; h) hv, benzene, r.t., 4h, 40%; i) $Bn(Me)_3N^+ICl_4^-$, AcOH, r.t., 3h, 41%

Scheme 1 . Total synthesis of the antibacterial AB002A from the cellular slime mold.

Another series of dibenzofurans was reported for its cytotoxicity towards HeLa human epithelial carcinoma cell lines. Kaniwa and his fellow ones isolated a novel series called Kehokorins A-C **4** from the fruit bodies of the myxomycete, Trichia favoginea var. persimilis.[4] Out of these, Kehokorin A was reported for its cytotoxicity against HeLa cells with an IC_{50} value of 1.5 µg/mL. The presence of rhamnose unit was credited for its cytotoxicity.

ANTIBACTERIAL ACTIVITY

The antibiotic resistance elements in the bacterial pathogens, has become the emerging and increasing problem for the researchers, policy makers and to the general public down these years. Many researchers have raised the topic to make new ways to curb the issues with pneumonia, tuberculosis, malaria and HIV-AIDS.[31–34] Discovery of the penicillin antibiotic in the late 1920s,[35] paved new way to the wound healing processes, but down the years its overuse has degraded that path due to the rise of drug resistant bacteria and super-bugs[36]. Thus, the need is to

work on the extraction of few biologically important molecules from the leaves of the Kielmeyera coriacea (Guttiferae). The biphenyl aucuparin and xanthones, found in the leaves was tested for their biological activity.[37] Phytochemical investigation of the dichloromethane extracts of K. coriacea leaves and stems has resulted in the isolation and identification of ten xanthones, one biphenyl (aucuparin, **5a**) and two triterpenes. Among these compounds the researchers also reported a dibenzofuran derivative **5b** 1,3,7- trihydroxy-2-(3-methylbut-2-enyl)-xanthone showed antimicrobial activities against Bacillus subtilis with MIC values of 12.5mg/ml, respectively.

Sawada and co-workers isolated a novel antibacterial substance from the cellular slime mold Dictyostelium purpureum K1001 in the year 2000. This was the first time when the fruiting bodies of this slime mold was utilized for the production of a new compound. After many structure determination studies on the hydrogenated derivative of this compound, it was finally confirmed that, 1,9-dihydroxy-3,7-dimethoxy-2-hexanoyl-4,6,8-trichlorodibenzofuran is the structure required **Scheme 1**.[30] The compound was renamed as AB0022A **8** and was confirmed for

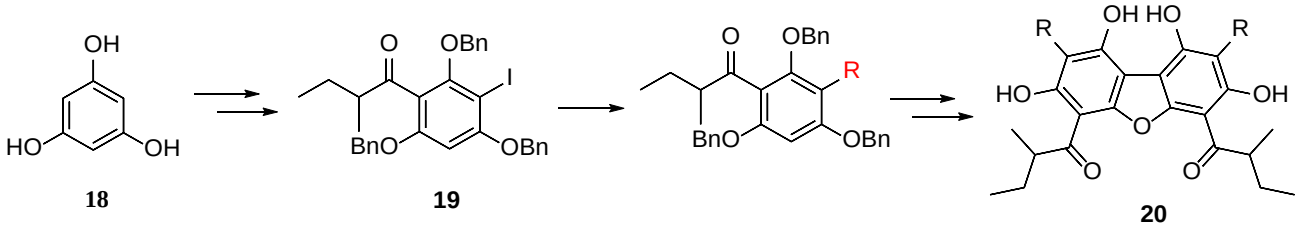


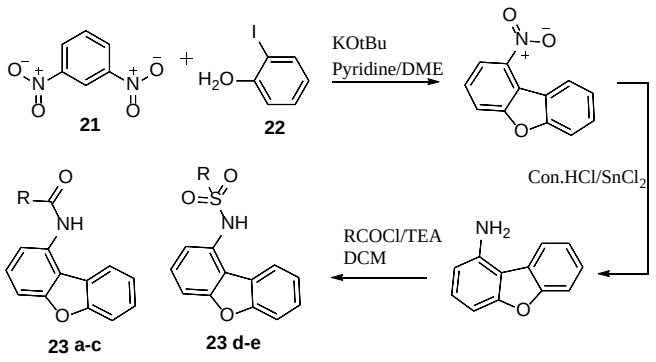
Figure 3. Biological active dibenzo furan containing antibacterial agents.

its biological activities involving inhibition of gram-positive bacteria Batillus subtilis and Staphylococcus aureus (MIC = 0.39- 50 µg/ml).

Rhodomyrtoxin C **6**, a biologically active dibenzofuran was synthesized from Pilidiostigma glabrum an Australian Myrataceae in the year 1983.[38] Shou et.al further studied about the anti-bacterial activity of the compound and reported that it shows activity against two different strains of *S. aureus* with MIC of 0.9 µM and 7.2 µM. The structurally similar Achyrofuran was also tested for its anti-bacterial activity.[39] When the compound was extracted from the aerial part of the plant and tested against the methicillin resistant and vancomycin-intermediate S.aureus strain NRS402, even the nanomolar concentrations, proved to be bacteriolytic by destroying 106 bacterial cells in 12hrs. Its anti-bacterial activity (MIC= 0.1 µM) was credited for its ability to compromise membrane impermeability of the cells.

Yet another antibacterial dibenzofuran was extracted from the Myrtus communis Linn; an evergreen sclerophyll shrub belonging to the Mediterranean flora, by Khan and co-workers in the year 2018[40]. The structure of the phloroglucinol derivative **7** was elucidated by 1-D, 2-D NMR and electrospray ionisation-high resolution mass spectrometer and finally reported to be 1,1' – (1,3,7,9- tetrehydroxydibenzo [b,d] furan-2,8-diyl)- bis (ethan-1-one). This Dbf derivative turned out to be highly bacteriolytic against both gram positive Staphylococcus aureus and gram-negative E.coli. Thus, its in-vivo, in silico and synthetic studies have been a working topic for the researchers.

In the year 2017, Royo and his co-workers published their work on the synthesis of new symmetric polyoxygenated dibenzofurans. The synthetic protocol **Scheme-2**[41] utilized phloroglucinol **18**, which was led to several reactions like monoacylation, iodination, Suzuki-Miyaura coupling, oxidative dimerization and regioselective cyclization to finally produce the required dibenzofurans **20** with 2-methylbutyril moieties at C-4 and C-6. The authors reported the high anti-bacterial activity of these compounds with lipophilic chains at C-2 and C-8 against the gram-positive bacteria including multi-resistant Staphylococcus aureus NRS402 and methicillin -sensitive Staphylococcus aureus ATCC25923.



R (a-c) =CH_3, C_6H_5, $C_{12}H_{10}$; R (d-e) = CH_3, $C_6H_5CH_2$

Scheme 3. Synthesis of 1-amino dibenzo [b,d]-furan derivatives using 1,3-dinitrophenol and iodophenol.

Shafi and co-workers synthesised a novel series of 1-amino dibenzo [b,d]-furan derivatives **23a-e** from the 1,3- dinitrophenol **21** and iodophenol **22** in the year 2019. After the structure elucidation of these compounds by ^{1}H and ^{13}C NMR, the antifungal and antibacterial properties were examined[42]. The compound **23c** demonstrated potent biological activity against the S. aureus bacteria and the fungi Candida albicans **Scheme 3**. Thus, its further pharmacological applications are being researched.

ANTIFUNGAL ACTIVITY

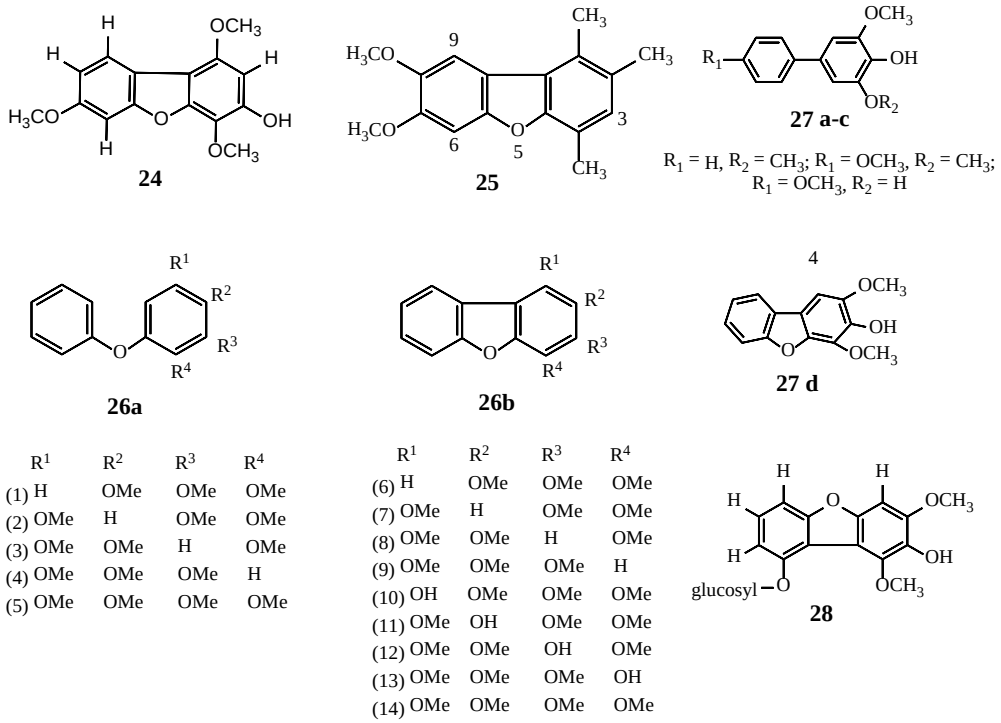
Among the 300 known human infecting species of fungi, there are about 25, which are known to be very common in the environment.[43] Even though, the presence of antifungal therapies like polyenes, flucytosine, azoles and echinocandins have been effectve to many fungal infections, but the parallel rise in immuncompromised population of the earth and the drug resistant fungi,[44] the invasive fungal infections are prevalent in the present times. Thus, there is need of more effective drugs, competitive strategies and efficient methods to counter the fungal infections.

In the year 2009, Shiu and co-workers published their work on the biological activity of the compounds extracted from the members of the genus Hypericum.[45] The extracted compounds were characterized by 1-D and 2D-NMR spectroscopy and mass spectroscopy. The new dibenzofuran **24** extracted from the H. revoltum ssp. Revoltum along with a pyranone, showed extensive medicinal properties. The authors had revealed that the mechanism of the action of this compound doesn't get affected by the multidrug resistant mechanisms of the most disease-causing bacteria strain; Staphylococcus aureus. The compound also proved to be acting as the major phytoalexins along with showing antifungal activity.

Further in the year 2014, Shi, Hu and co-workers published their work on the medicinal activity of a traditional Chinese plant; Ligularia caloxantha[46]. The authors identified that the presence of benzofuran and dibenzofuran derivatives along with few triterpenes has the key role in the medicinal properties of the plant. Further they reported that the dibenzofuran derivatives present in the root parts of this mountainous plant, has the key role in the healing of cuts and wounds. The said compound **25** was also proved to give the antiascarid activity to this medicinal plant.

By studying the challenging mechanisms of the Photinia davidiana and the Pyracantha plants, Kokubun and the co-workers realized that these plants produced two different dibenzofurans as the phytoalexins to fight against the plant pathogens. The antifungal properties of the newly identified dibenzofurans, 7-methoxyeriobofuran and the 9-hydroxyeriobofuran was deeply discussed in their work, published in the year 1995.[47]

The wood of Pyrus communis L. (perry pear trees) was subjected to the research and finally was determined to have the antifungal compounds α-pyrufuran and β-pyrufuran. The research was carried out in the year 1983 by Kemp and co—workers.[48] The Spectroscopic and chemical evidence showed that



	R1	R2	R3	R4
(1)	H	OMe	OMe	OMe
(2)	OMe	H	OMe	OMe
(3)	OMe	OMe	H	OMe
(4)	OMe	OMe	OMe	H
(5)	OMe	OMe	OMe	OMe

	R1	R2	R3	R4
(6)	H	OMe	OMe	OMe
(7)	OMe	H	OMe	OMe
(8)	OMe	OMe	H	OMe
(9)	OMe	OMe	OMe	H
(10)	OH	OMe	OMe	OMe
(11)	OMe	OH	OMe	OMe
(12)	OMe	OMe	OH	OMe
(13)	OMe	OMe	OMe	OH
(14)	OMe	OMe	OMe	OMe

Figure 4. Biological active dibenzo furan containing antifungal agents.

the compounds are 1,2,3,4-substituted trimethoxydibenzofuranols **26a-b**. These dibenzofurans were also analysed for their biological activity and was confirmed to have potent phytoalexin behaviour.

Two phytoalexins were synthesized from the diseased shoot and leaves of loquat (Eriobotrya japonica: Rosaceae) plant called aucuparin **27a-c** and eriobofuran **27d**. The researchers Watanabe and co-workers published their work in the year 1990,[49] which highlighted the antifungal activities of these compounds. Their research on these phytoalexins further led to the isolation of the two antifungal principles, 4'-methoxyaucuparin and rhaphiolepsin.

Research was carried out by Geza and co-workers in the year 1997, to investigate the Phytoalexin Production in an Apple Cultivar Resistant to Venturia inaequalis. With this research it was concluded that the major compound produced by scab-resistant cells in response to the challenge by the fungus, has been identified as the 2,4-methoxy3-hydroxy-9-O-β-D-glucosyloxydibenzofuran by UV, mass spectrometry, 1H-nuclear magnetic resonance (NMR), and 13C-NMR spectroscopy.[50] The dibenzoderivative (Malusfuran) **28** production within the plant, is one of the many components of the resistance principle of apples against V. inaequalis.

ANTIMALARIAL ACTIVITY

According to the WHO, Malaria is a life-threatening disease caused by the Plasmodium parasites. These parasites are carried into the human body via the infected female Anopheles mosquitoes. Out of the 5 different species of parasites, Plasmodium falciparum and Plasmodium vivax are considered to be the deadliest and unfortunately, dominant parasite species across many countries.[50] Although there are appreciable number of drugs and insecticides being present in the market for the cure and prevention of the disease, but as the danger of parasites getting resistance towards them is hanging around the neck,[51] the research of new and also environment friendly compounds is the need of hour. The below section specially involves some Dbf derivatives being utilized for the synthesis of anti-plasmodial agents.

Talontsi.et.al isolated two unusual dibenzofurans called Preussiafurans-A and B from the fungus Preussia sp, present in Enantia Chlorantha Oliv, along with other 6- known compounds in the year 2014.[52] These Dbf derivatives were structurally elucidated by 1-D, 2-D NMR and HR-ESIMS. Upon the estimation, the authors reported that the Preussiafuran A **29a** with a carboxylic group at C-8 has more potent biological activity towards the chloroquine resistant strain NF_{54} of malaria parasite P.falciparum with MIC_{50} = 8.76µM. Moreover, the other substituent Preussiafuran B **29b** with a hydroxylated group, showed higher cytotoxicity on L6 cell lines.

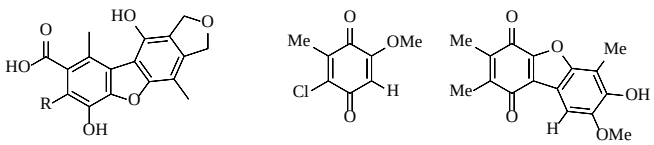


Figure 5. Biological active dibenzo furan containing antimalarial agents.

An Endophytic fungus, Xylaria sp, was utilized by Tansuwan and fellow workers in 2007, to isolate 2-chloro-5-methoxy-3-

methyl cyclohexa-2,5-diene-1,4-dione **30** and Xylariaquinone A **31**.[53] The novel compounds had their structure confirmed by the spectroscopical data and single crystal X-ray data. Under the study by microculture radioisotope technique,[54] the authors reported that, both the compounds have in-vitro antiplasmodal activity against the multidrug resistant strain Plasmodium falciparum K1. However, when the IC_{50} values of both the compounds 1.84 and 6.68 µM were reported respectively, the lower activity of the dibenzo derivative was observed. With an addition of cytotoxic activity against the African green monkey kidney fibroblasts, both the compounds are further being studied foe their efficient use.

ANTIALLERGIC ACTIVITY

In the year 2008, Dai and co-workers reported their work on the extraction of dibenzofuran derivatives from the fruit of Pyracantha fortuneana.[55] They isolated several dibenzofuran glycosides and fortuneanosides G-L **32a-f** from this fruit. These compounds were then subjected to the analysis for their various medicinal activities. The further reported that the Fortuneanosides G—J **32a-d** showed more potent tyrosinase-inhibitory activity than arbutin.

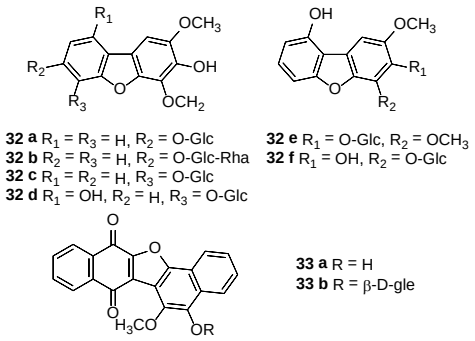


Figure 6. Biological active dibenzo furan containing antiallergic agents.

Impatiens balsamina L. a Chinese medicinal plant, known for its traditional use in the treatment of varied number of ailments like articular rheumatism, bruises, beriberi[56] and several types of dermatitis.[57] It is also known to possess antianaphylactic,[58–60] antipruritic,[61] and antihistamic[62] activities. This magically medicinal plant was once again proved to have additional medicinal activity. Ishiguro et al. synthesised two novel dinapthofurans, balsaminone A **33a** and balsaminone B **33b** from the pericarp of the fruit of this plant[63]. On further evaluation, both the compounds showed potent antipruritic activity in mice. Thus, its anti-allergic properties are under further studies, whereas its anti-tumor activity[64] against MCF-7, HeLa, HCT-116 and HT-29 cell lines is already reported.

OTHER ACTIVITIES- ANTI-HIV-1 AGENT, ANTI-HYPERGLYCEMIC, ANTI-PLATELETS, ANTI - INFLAMMATORY

The first acquired immunodeficiency syndrome (AIDS) patient was found in the US in 1981. After that therapy for HIV-1 infection & AIDS has been used very rapidly.[65,66] Within 10 years of the identification of the virus, the first drug, zidovudine was developed.[67,68] After that a lot of drugs were developed for this virus.

Fan and co-workers carried out their study on the synthesis of human immunodeficiency virus-1 inhibiting in-vitro dibenzofurans, for the very first time in the year 2009.[69] Out of the 10 compounds synthesised by the team, the four compounds were proved to have potent anti-HIV activity on evaluation. The compounds with cyano group on the 2nd position and the presence of electron withdrawing groups like fluoro and nitro group, increased the potency of the dibenzofurans. Finally, the four dibenzofurans **34, 35, 36, 37** were reported to have high activity with EC50 values of 12.52, 15.32, 12.99 and 18.57 µg/ml and TI values of >16.18, >13.10, >11.39 and >11.07 respectively.

The conversion of dietary starch and other complex carbohydrates into simple sugars by the gastrointestinal enzymes, is inhibited by the action of anti-hyperglycemic drugs. The blood sugar levels are nightmares for the diabetes-milletus patients. These drugs tend to control the same.

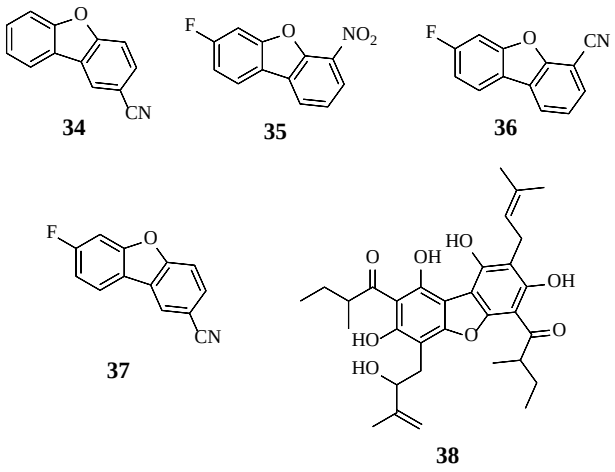


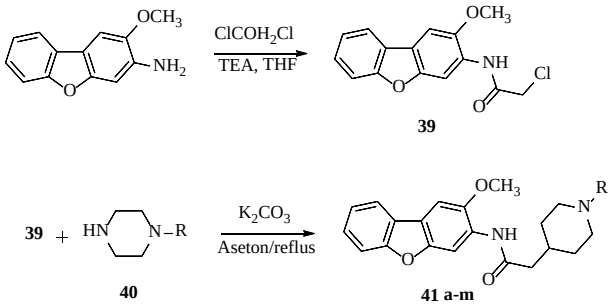
Figure 7. Biological active dibenzo furan containing anti-HIV-1, anti-hyperglycemic, anti-platelets, anti-inflamatory agents.

In the year 2001, Carney and co-workers published their work on the compounds derived from the Achyrocline satureioides; a South-American medicinal plant.[70] The bioassay guided fractionation led to the derivation of a new prenylated dibenzofuran called Achyrofuran **38**. This compound led to many changes in the world of non-insulin dependent diabetes mellitus. The active compound **38** was isolated from the components of the plant, after several processes including the LH-20 chromatography. The derived achyrofuran was proved to have significant antihyperglycemic activity in an in vivo type 2 diabetes mouse model.

The cyclooxygenase-1 (COX-1) enzyme acts as a platelet activator by generating thromboxane A2.[71] The platelet aggregation leads to thrombus formation which ultimately causes issues like coronary artery disease, cerebrovascular accidents and peripheral arterial disease.[72] The anti-platelet therapy involves inhibition of COX-1 enzyme to prevent the platelet aggregation

in the blood vessels and blockage of blood flow to the body tissues.

The reaction of N-(2-methoxy-3-dibenzofuranyl)-2-chloroacetamide **39** with the substituted piperazine **40** derivatives led to the formation of a novel series of dibenzofuran-piperazine derivatives **41 a-m**. The research carried out by the authors Yurrtas and co-workers in the year 2015, shed new light in the field of platelet activation and aggregation chemistry and finally leading towards more competent, efficient antiplatelet drugs with less chances for side effects like gastric erosion, agranulocytosis, neutropenia, thrombocytopenia, aplastic anemia and so on.[73] Out of many products of the reaction, the dibenzofuran with 2-furoyl **41m** substituent proved to be possessing high percentage inhibition as much as the standard drugs utilized in the similar purpose like aspirin, ridogrel, and dipyridamole on arachidonic acid induced platelet aggregation. The structure of the compound N- (2-methoxy-3-dibenzofuranyl)-2-[4-(2-furoyl) piperazin-1-yl] acetamide was characterized by ^{1}H NMR, ^{13}C NMR, mass spectral data, elemental analysis and HPLC analysis.



41 a-m ; R = CH_3, Ph, 2-CH_3Ph, 3-CH_3Ph, 4-CH_3Ph, 2-OCH_3Ph, 3-OCH_3Ph, 4-OCH_3Ph, $-$-NO_2Ph, 2-Pyridyl, 2-Pyrimidyl, Benzyl, 2-Furoyl respectively.

Scheme 4: Total synthesis of dibenzofuran-piperazine series.

Four new dibenzofurans were isolated from the extract of the roots of Rhaphiolepis indica var. tashiroi.[7] It is one of a variety of an evergreen shrub found in Taiwan, and also in many parts of Asia.[74] The root extract of the plant was tested positive for the anti-inflammatory activity. This was the alarming tone for the researchers to look for the chemical constituents of the plant. Out of a large number of dibenzofurans and biphenyls extracted from it, 2-hydroxy-3,4,6,9-tetramethoxydibenzofuran was determined to have potential anti-inflammatory activity. When compared with several other agents, this dibenzofuran derivative delivered more biological activity than the known anti-inflammatory agents like Eucidafuran and aucuparin.

CONCLUSION

In summary we can easily state that the use of dibenzofurans and their derivatives as the biologically active complexes in the medicinal field has grown extensively. The outstanding results of some experiments which are mentioned above, clearly give an idea of the enhancing demand for these complexes. The comparisons of these complexes with the other drugs and agents used in the similar field otherwise, give a positive point to these complexes having similar or even better performance. Moreover, from the above data it can clearly be seen that, most of the dibenzofuran derivatives are either be isolated or derived from the natural products with least cost of synthesis, owing to their greener upper hand. The arising scope of Dbfs in the field of anticancer, anti-bacterial, anti-fungal, anti-hyperglycemic, anti-allergic and as anti-HIV agents can give more influencing results upon experimentation on these scaffolds. This review is directed to give better information for the synthesis of more accurate molecules with better biological properties and also to encourage development of better synthetic methods.

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