CHAPTER II

REVIEW OF LITERATURE

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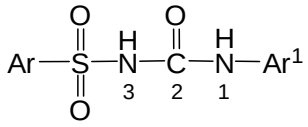
2.1 INTRODUCTION

Synthesis of the molecules that are important in the control of aging diseases are important in the present decades. The compounds like Diarylsulfonylurea-chalcone may act as anti-inflammatory agents that may be link to several diseases.

2.2 DIARYLSULFONYLUREA

Diarylsulfonylureas **(1)** are the derivatives of urea (NH_2CONH_2) with arylsulfonyl group in the position 3 and an aromatic or heteroaromatic ring at the position 1. Sulfonylureas became widely available since 1955 as popular oral hypoglycemic drugs in medical performance considers action of diabetes type 2 characterized for their insulin secretagogue property (e.g., Glibenclamide **(2),** Gliclazide **(3)** and Glimepiride **(4)**. These drugs combine toward the sulfonylurea receptor SUR1 on the β-cells, triggering the closure of the nearby potassium channel, which in turns leads the β-cell to increase insulin secretion (Krentz and Bailey, 2005; Garber, 2000; Lindblad and Melander, 2000; Quayle and Standen, 1994; Amoroso et al., 1990; Reis and Velho, 2002).

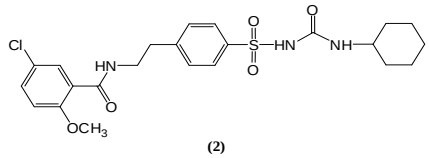


(1)

Sulfonylureas are crystalline solids of acidic character. Their solubility in water and the common organic solvents varies with the complexity of their chemical structure, compounds containing free urea grouping (i.e. $R\text{-}SO_2NHCONH_2$) may often be crystallized from boiling water; sulfonylureas containing additional substituent (i.e.

R-SO_2NHCONH-R^1) are usually soluble in polar solvents, less so in hydrocarbon solvents, and sparingly soluble in water (Frederick, 1951).

The synthesis of compounds containing diarylsulfonylurea moiety has been a subject of extensive research in the recent past because of their importance as drugs, and for other applications in pharmaceutical and in agrochemical fields (Khodair, 2001; Jakse et al., 2001). In addition to their major hypoglycemic activity, diarylsulfonylureas also possess enormous potential as cancer chemotherapeutic agents. The antitumor potential of diarylsulfonylureas was pioneered by the discovery of sulofenur **(5)**. The molecule sulofenur (LY186641) is a diarylsulfonylurea, a new class of antineoplastic agent which showed significant cytotoxicity in the clinical trials against lung, breast, colon, ovarian, pancreatic, renal, and gastric cancers. These distinctive properties make diarylsulfonylurea a valuable pharmacophore for drug discovery and development (Medina et al., 1998; Medina et al., 1999; Mastrolorenzo et al., 2000).



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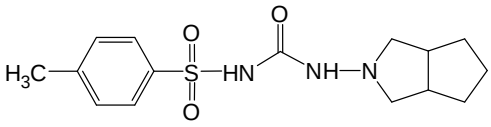

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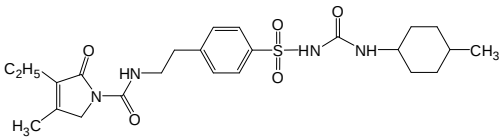

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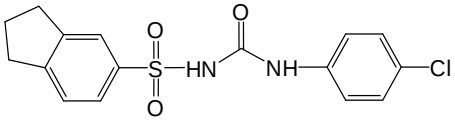
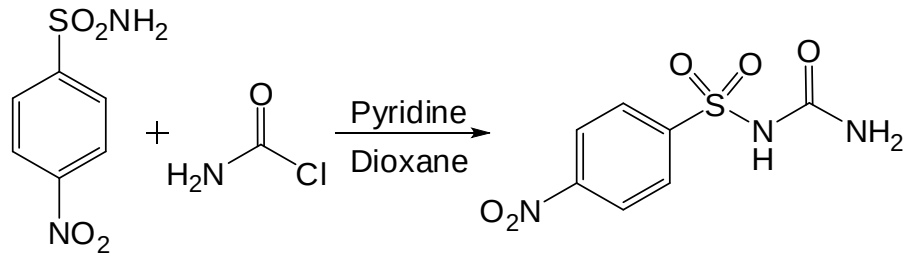


(5)

2.2.1 Preparation of Diarylsulfonylureas

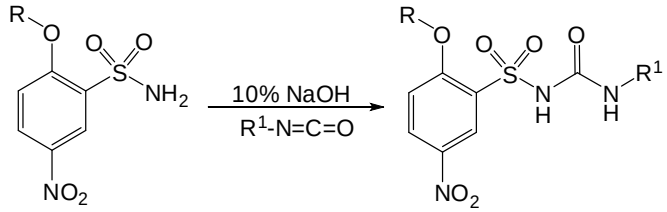
A number of established protocols are there for the synthesis of diarylsulfonylurea moiety, which can be well modified to prepare a number of differently substituted diarylsulfonylureas. Some of the conventional methods are given below.

1) 4-Nitrobenzenesulfonamide reacts with carbamyl chloride in dioxane solution in the presence of pyridine to yield 4-nitrobenzenesulfonylurea (Scheme 2.1) (Howbert et al., 1990).



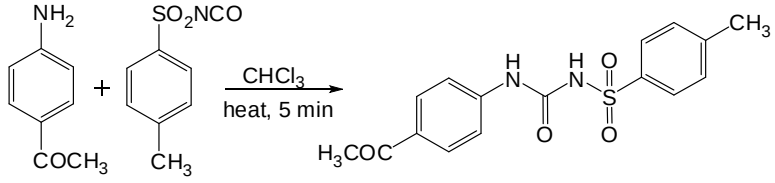
Scheme 2.1

2) Deprotonation of the sulfonamide group of compounds followed by reaction with the appropriate aromatic or aliphatic isocyanate led to the synthesis of sulfonylurea derivatives (Scheme 2.2) (Hanson et al., 2007).



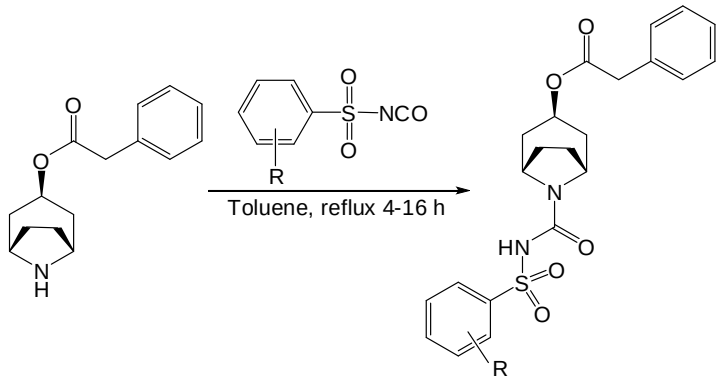
Scheme 2.2

3) The reaction of 4-aminoacetophenone with *p*-tosylisocyanate in chloroform, gives 1-(4-acetylphenyl)-3-tosylurea (Scheme 2.3) (Leon et al., 2007).



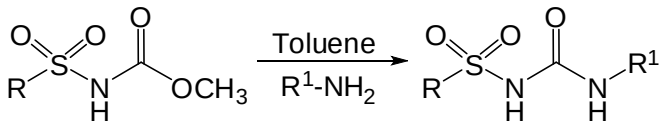
Scheme 2.3

4) Secondary amine, on refluxing with substituted sulfonylisocyanates in toluene for 4-16 h, gives sulfonylurea (Scheme 2.4) (Lehr et al., 2005).



Scheme 2.4

5) Diarylsulfonylureas can also be synthesized in good yields by refluxing equimolar amounts of substituted or unsubstituted sulfonylurethanes and primary amine in toluene (Scheme 2.5) (Ameya and Nandini, 2007).



Scheme 2.5

2.2.2 Molecular Spectroscopy of Diarylsulfonylureas

2.2.2.1 Ultra Violet Spectroscopy

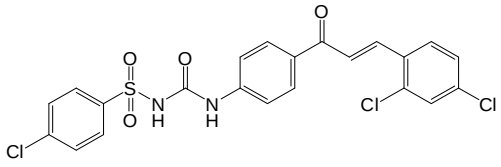
Ultraviolet absorption spectrum of gliclazide **(3)** in dichloromethane solvent was shown absorption maximum (λ_{max}) at about 232 nm (Penderjit et al., 2011).

2.2.2.2 Infra Red Spectroscopy

Infrared (IR) spectral studies of sulfonylureas showed that the characteristic bands attribute to the sulfone (O=S=O) group occur at frequencies 1160-1120 cm^{-1} and at 1350-1300 cm^{-1}**,** these bands are very intense and show splitting. The NH stretching frequencies of secondary amines show only a single stretching band in the 3500-3200 cm^{-1} region. The *N*-alkylated compounds show two or more bands at 3500-3100 cm^{-1}. The secondary amides (amide I & II band) show also another strong absorption band which has a frequency range of 1570-1515 cm^{-1} for the compounds examined in the solid state (Bellamy, 1962; Nitta and Ando, 1962).

2.2.2.3 Nuclear Magnetic Resonance Spectroscopy

Leon *et al*. 2007 studied the ^{1}H NMR and ^{13}C NMR spectra of a series of sulfonylurea derivatives. The ^{1}H NMR spectrum of **(6)** exhibit characteristic peaks of NH protons as broad singlet at δ 9.06 ppm and followed by Hα and Hβ protons as two doublets one at δ 7.37 (*J*=15.58 Hz) and the other one at δ 7.88 (*J*=15.58 Hz) ppm respectively.

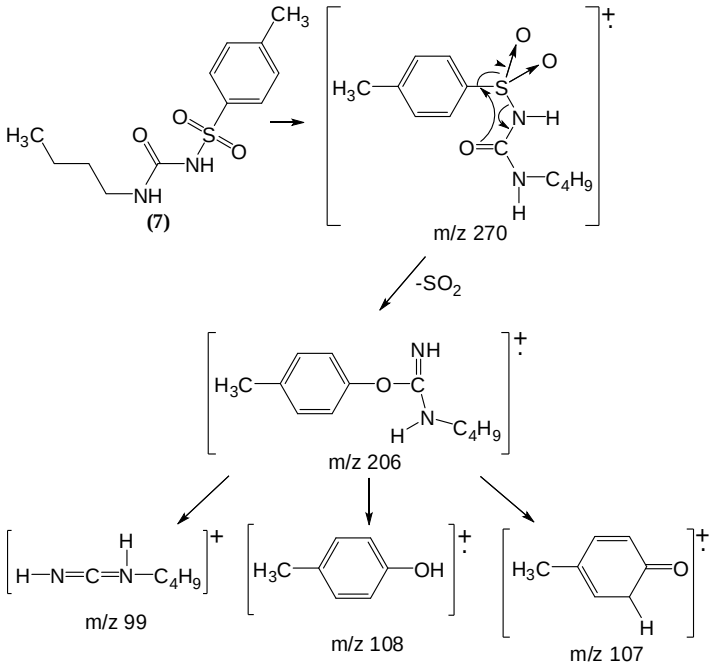


(6)

In the ^{13}C NMR spectrum of **(6)**, the chemical shifts of the carbon atoms have been assigned correspondingly at δ 158.83, δ 187.40, δ 126.18 and δ 148.31 ppm indicating the presence carbonyl carbon (CO) of sulfonylurea group, carbonyl carbon (CO), Cα and Cβ of α,β-unsaturatedketone group respectively (Leon et al., 2007).

2.2.2.4 Mass Spectroscopy

The molecular ion peak in the electron impact mass spectrum (EI-MS) of tolbutamide **(7)** is observed at *m/z* 270. The fragmentation pattern of tolbutamide may be represented as in Scheme 2.6 (Marvin et al., 1966).



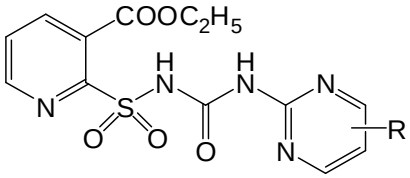
Scheme 2.6

2.2.3 Biological Activity of Diarylsulfonylureas

The compounds with diarylsulfonylurea moiety in its chemical structure have been reported to possess different biological and pharmacological activities such as antimicrobial, anticancer, antimalarial, antitubercular, antiviral, antihyperglycemic, and herbicidal activities etc. Thus diarylsulfonylureas continue to attract considerable scientific interest because of their association with a variety of biological activities. Given below is a brief account of substituted sulfonylureas, which resulted in showing a range of biological and pharmacological activities.

2.2.4 Anticancer Activity

Gil *et al.* have prepared a series of some new N-(2-pyridylsulfonyl) urea derivatives **(8)** and evaluated for their *in vitro* cytotoxicity against human cancer cell lines. Among the series of compounds tested, the compound **(9)** displayed significant cytotoxicity against HT-29, K-562 and HTB-54 tumor cell lines. Structural modifications on aryl systems affected differently to the cytotoxicity activity against each cell line (Gil et al., 1999).



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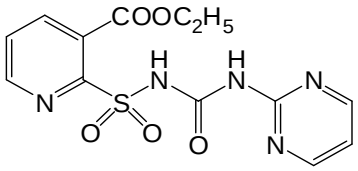
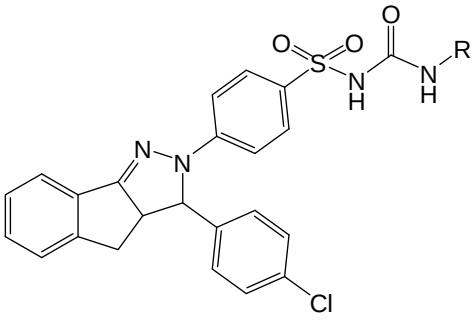


(9)

Rostom *et al.* have synthesized a set of 3-(4-chlorophenyl)-[1,2-c]pyrazolines substitute through sulfonylurea **(10)**. New synthesized target compounds were subjected into the NCI-*in vitro* disease-oriented antitumor testing as part of estimation for their antitumor activity. Compound **(11)** shows potential wide spectrum antitumor action against the examined subpanel tumor cell position (GI_{50} < 100 μM) (Rostom et al., 2006).



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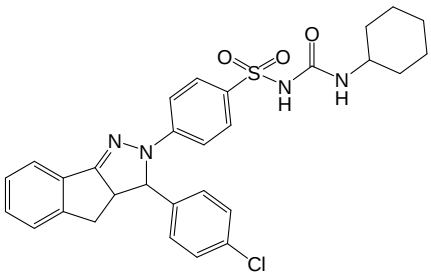
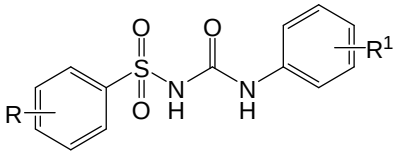


(11)

Howbert *et al.,* 1990 have designed and synthesized a series of diarylsulfonylureas **(12)** with exceptionally broad-spectrum activity against syngeneic rodent solid tumors *in vivo*. Their discovery resulted from a program dedicated to *in vivo* screening for novel oncolytics in solid tumor models, rather than traditional ascites leukemia models. The structures, oral efficacy, side-effect profile, and mechanism of action of these sulfonylureas appear to be distinct from previously known classes of oncolytics. An extensive series of analogues was prepared to probe structure-activity relationships (SAR), with particular focus on the substituent patterns of each aryl domain. Quantitative analysis of these substituent SARs, using the method of cluster significance analysis, showed the lipophilicity of the substituents to be the dominant determinant of activity. One compound from the series, LY186641 **(13,** sulofenur**)**, has progressed to Phase I clinical trials as an antitumor drug (Howbert et al., 1990).



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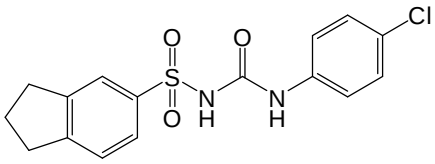
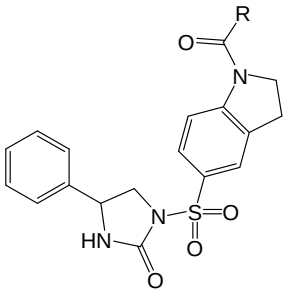


(13)

Jung et al., 1998 have prepared a series of some novel 4-phenyl-1-arylsulfonyl-imidazolidinones **(14)** and screened for their cytotoxicities. Among them compound **(15)** displayed much more potent cytotoxicity than doxorubicin and highly effective antitumor activity against murine (3LL, colon 26) and human xenograft (NCI-H23, SW620) tumor models (Jung et al., 1998).



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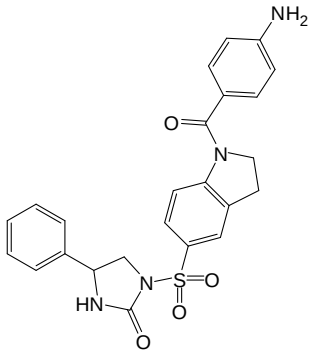
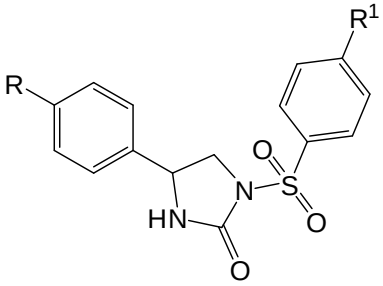


(15)

Jung *et al., 1996* have synthesized a series of some novel arylsulfonylimidazolidinones **(16)** and **(17)** containing sulfonylurea pharmacophore and evaluated for their *in vitro* cytotoxicity against human cancer cell lines. The most potent compound **(18)** was evaluated for antitumor activity in mice (C3H/He) bearing murine mammary adrenocarcinoma (MM48). Compound **(18)** showed 80-90% suppression of tumor growth at the dose of 300 mg/kg/day (Jung et al., 1996).



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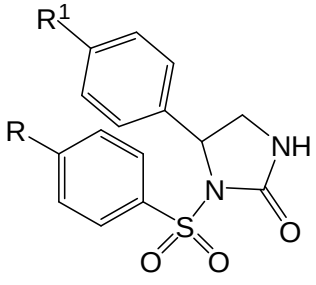

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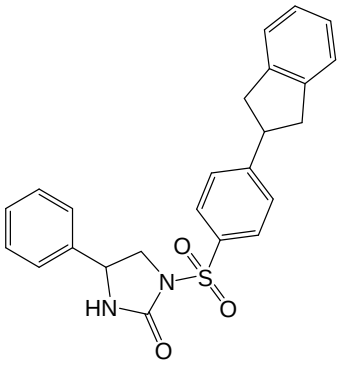
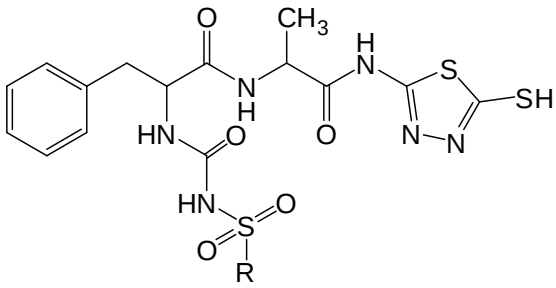


(18)

Scozzafava and Supuran, 2002 reported the designed and synthesized a novel set of sulfonylureas **(19)** consisting 1,3,4-thiadiazole moiety and screened for their inhibitory activity against selected proteases. These new compounds were assayed as inhibitors of human MMP-1, MMP-2, MMP-8 and MMP-9, and of the collagenase isolated from the anaerobe *Clostridium histolyticum* (ChC). The new derivatives **(20)**, **(21)**, **(22)**, **(23)** and **(24)** proven to be potent inhibitors to the metalloproteases, with actions in the lower micromolar variety for several target enzymes, depending upon the substitution prototype at the arylsulfonyl (ureido) moiety (Scozzafava and Supuran, 2002).



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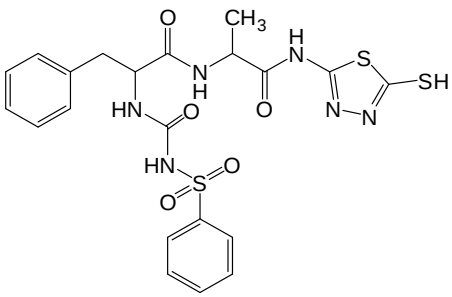

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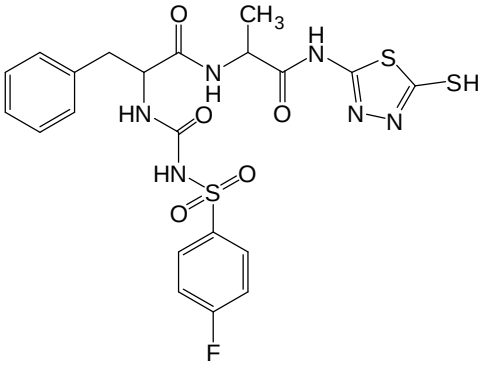

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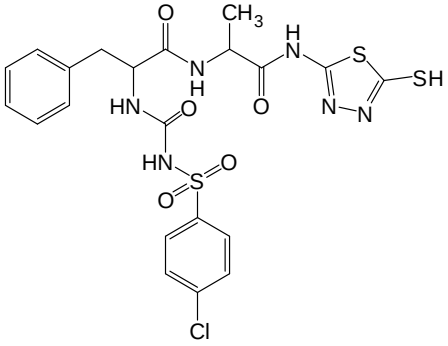

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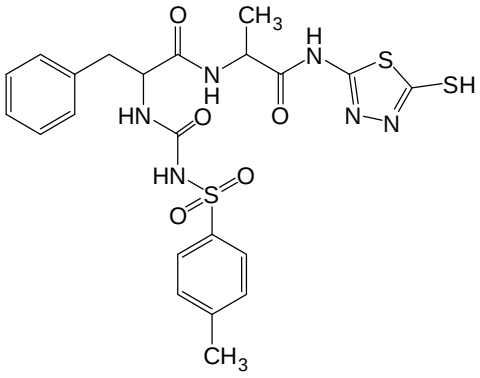

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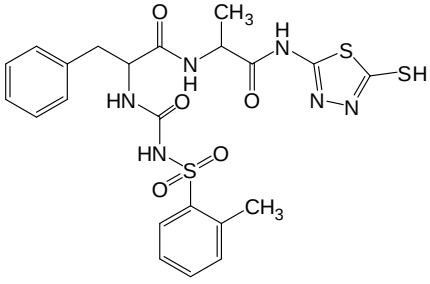
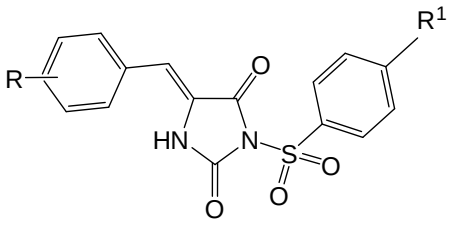


(24)

El *et al.,* 2010 have synthesized a set of novel cyclic arylsulfonylureas and examined for their antitumor action against 60 tumor cell lines in use from 9 similar organs. The tested compounds were shown fine inhibitory result at the ovarian cancer (IGROV1) cell line. A major inhibition for (RXF393) renal cancer cells were identified with set **(25)** compounds, whereas in the further two sets **(26)** and **(27)**, there was a considerable inhibition of melanoma cells (SK-MEL-2) and ovarian cancer cells (OVCAR-8).Thoroughly, by the significant inhibition of molecule **(28)** to RXF393 and IGROV1 cells, a immense inhibition (199.62%) for (M14) Melanoma cells was identified at the screened concentration (10 µM). pharmacophore and ADME-T prediction methods were use to revise the antitumor activity of the active molecules and to categorize the structural modes necessary for antitumor activity (El *et al.,* 2010).



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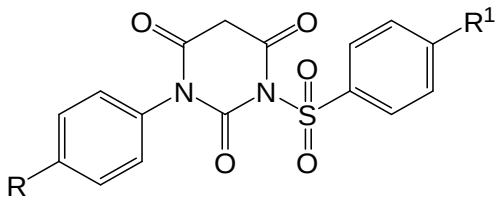

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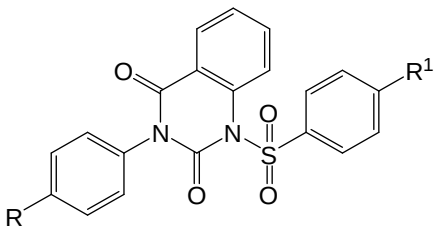

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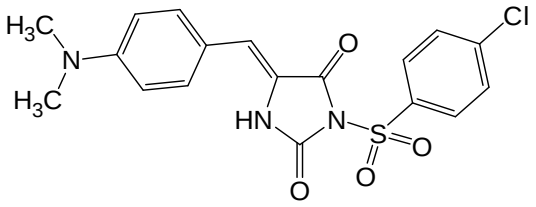
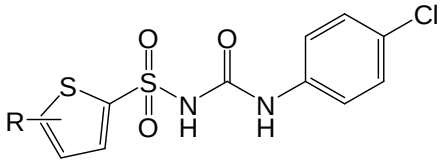


(28)

Mohamadi *et al.,* 1992 have designed and synthesized a series of diarylsulfonylureas **(29)** as new class of cancer chemotherapeutic agents and evaluated against subcutaneously implanted 6C3HED lymphosarcoma. The diarylsulfonylurea **(30)** as representative member of this series exhibited significant efficacy against tested cancer cell line (Mohamadi *et al.,* 1992).



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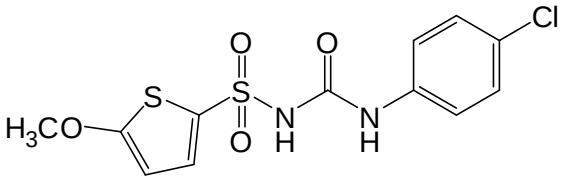
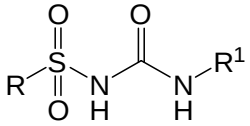


(30)

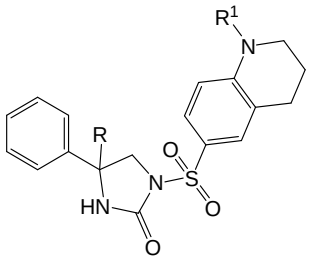
Toth *et al.,* 1997 have synthesized a series of oncolytic diarylsulfonylureas **(31)** for *in vitro* cytotoxicity activity against CEM cells, *in vivo* antitumor activity against subaxillary surrounded 6C3HED lymphosarcoma and metabolic break to the 2-sulfate of 4-chloroaniline. In general, several analogs demonstrated excellent growth inhibitory activity in the 6C3HED model when dosed orally or intraperitoneally (Toth *et al.,* 1997).



(31)

Subramanian *et al.,* 2011 have prepared a series of some novel cyclic sulfonylurea derivatives **(32)** and evaluated for their murine leukemia (P288D1) cell line and *in vitro* anticancer activity against 5 human tumor cell lines, including KATO III, K562,

SK-OV-3, COLO205, A549. Some compounds, **(33)** and **(34)** exhibit similar *in vitro* anticancer action to doxorubicin against K562 A549, and KATO III cell lines and proved greater xenographic consequences against SW620 and NCI-H23 cancer cell positions (Subramanian *et al.*, 2011).



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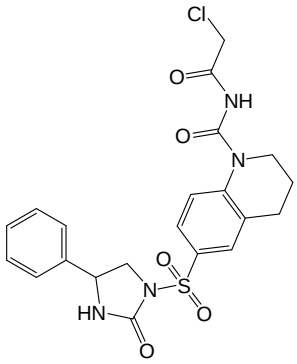

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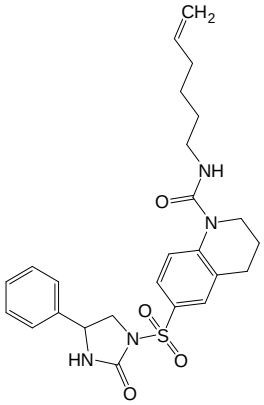
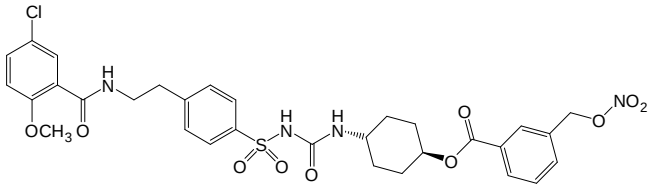


(34)

2.2.5 Antidiabetic Activity

Calderone *et al.* 2009 reported the hybrid drugs **(35)** and **(36)**, nitrooxymethylbenzoate-derivatives of 4-trans-hydroxy-glybenclamide **(37)**. The pharmacodynamic characterization of **(36)** showed that its diabetic activity is enrich with other NO-donor effects, conferred vasorelaxing and thrombocyte properties of potential efficacy for diabetes-related through cardiac disorder (Calderone *et al.*, 2009).



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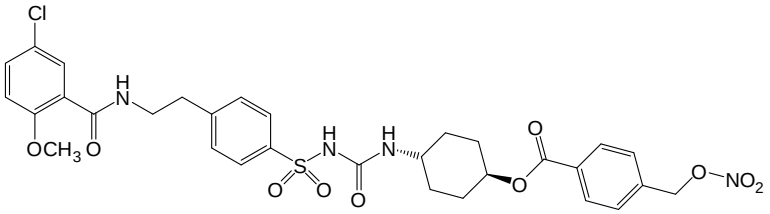

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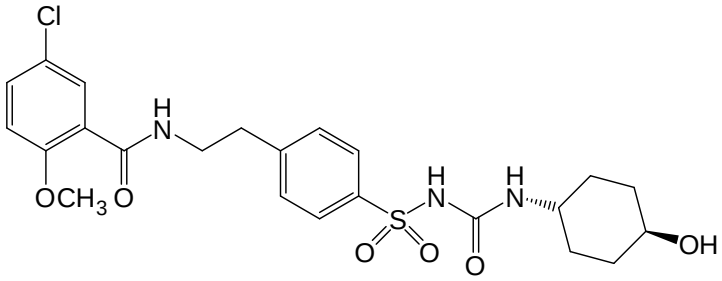
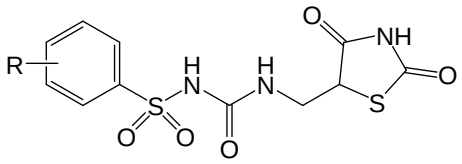


(37)

Jawale *et al.,* 2012 have synthesized a series of some new sulfonylureas **(38)** consisting 2,4-thiazolidinedione moiety. The newly synthesized compounds were evaluated for the antihyperglycemic activity in the normal rats model and among the compounds **(39)**, **(40)**, **(41)** and **(42)** showed a significant antihyperglycemic activity in the sucrose loaded rat model (Jawale *et al.,* 2012).



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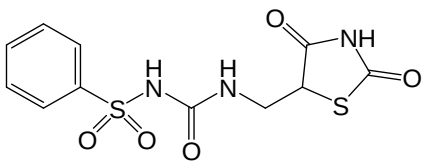

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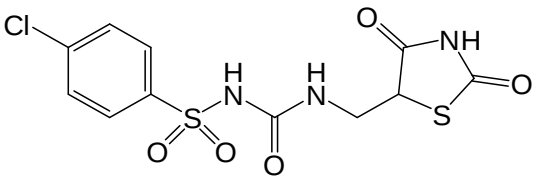

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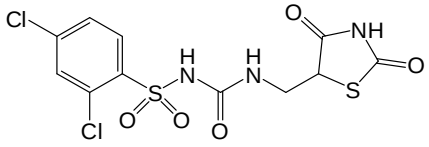

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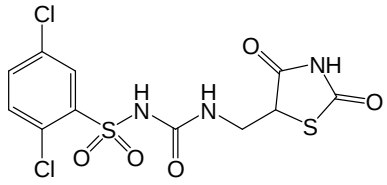
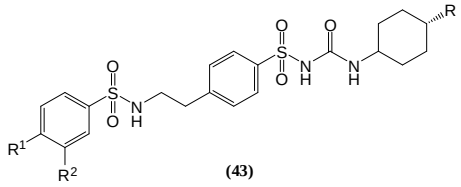


(42)

Zhang *et al.,* 2009 have designed and synthesized a series of novel class of sulfonylurea derivatives **(43)** substituted with benzenesulfonamide set. The mark compounds were tested for the possessions on the insulin outflow of separated rat pancreatic islets and the glucosic carrying in adipocytes of mice. Some Compounds shows good potency. Compound **(44)** also had strong antiplatelet action and shows an tremendous property to defend collagen–epinephrine-induced rats mortality as fine as plasma glucose-lower activity in animals. The primary pharmacological report of compound **(44)** shows that it may be valuable in diabetics with cardiovascular and nephropathy complications (Zhang *et al.*, 2009).



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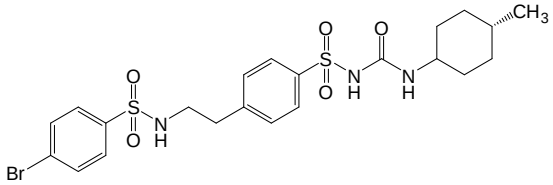
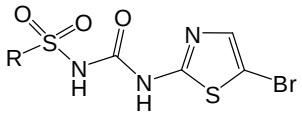


(44)

Kitas *et al.,* 2010 have discovered a series of sulfonylureas **(45)** and evaluated as a new class of potential fructose-1,6-bisphosphatase (FBPase) inhibitors. Compound **(46)** showed favorable ADME properties, for example, F = 70%, and a robust 32% glucose reduction in the acute *db/db* mouse model for Type-2 diabetes (Kitas *et al.,* 2010).



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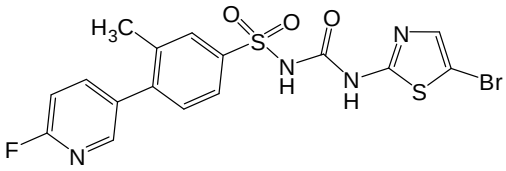
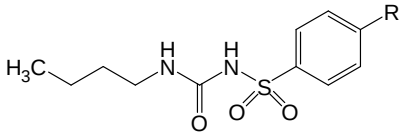
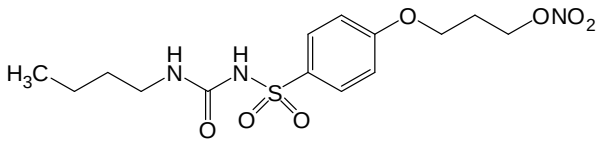


(46)

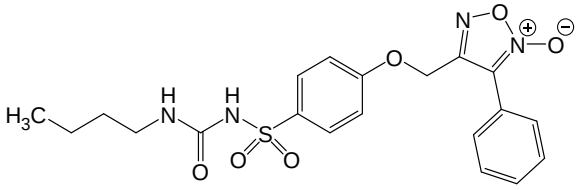
Tamboli *et al.*, 2012 have described a new class of NO-donor hypoglycemic products **(47)** obtained by joining tolbutamide, a typical hypoglycemic sulfonylurea, with a NO-donor moiety through a hard link. A preliminary biological characterization of these compounds, including stimulation of insulin release from cultured rat pancreatic β-cells and *in vitro* vasodilator and anti-aggregatory activities, is reported. Compounds **(48)**, **(49)**, and **(50)**.The tolbutamide compound is connected with substructures that exhibit mild or moderate NO-dependence vasodilator action, emerge as model for which supplementary *in vivo* tests would be useful, as they are significantly functional to treat diabetes (Tamboli *et al.*, 2012).



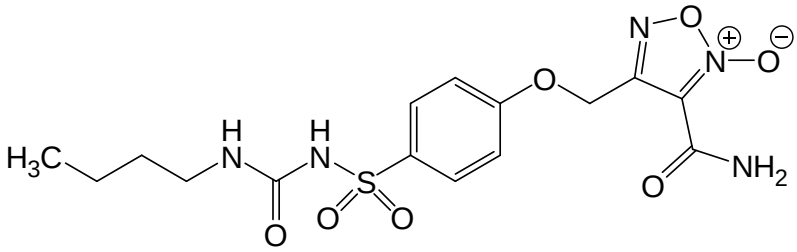
(47)



(48)

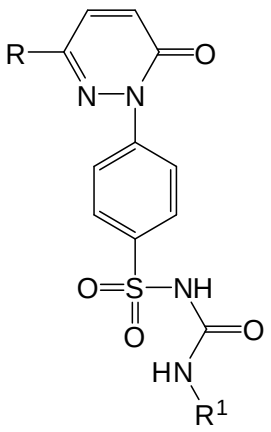


(49)



(50)

Rathish *et al.,* 2009 have synthesized a series of some novel pyridazinone substituted benzenesulfonylurea derivatives **(51)**. The blood sugar lowering levels of sulfonylurea derivatives using glucose tolerance test at the dose of 20 mg/kg (p.o.) were evaluated in normal and NIDDM (n2-STZ) rat models. Almost all the compounds are completely prevented the rise of blood glucose levels of NIDDM rats as compared with NIDDM control, while compounds **(52)** and **(53)** was showed more than 50% prevention observed in the rise of blood glucose levels. In glucose-fed normal rats, the compounds at the similar dose except **(54)** is significantly prevented the rise of blood glucose (more than 50%) when compared with the control of glucose-fed normal rats. The results showed evident that all the compounds was exhibited considerably potent blood glucose lowering activity and also may be used as lead compounds for the developing novel anti diabetic drugs (Rathish *et al.,* 2009).



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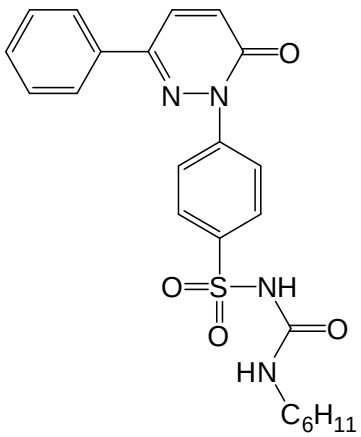

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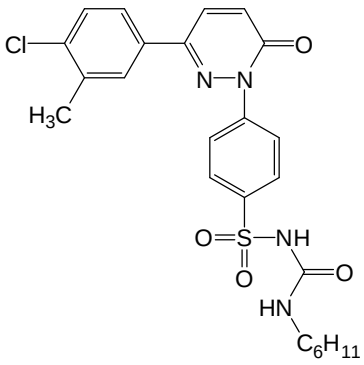
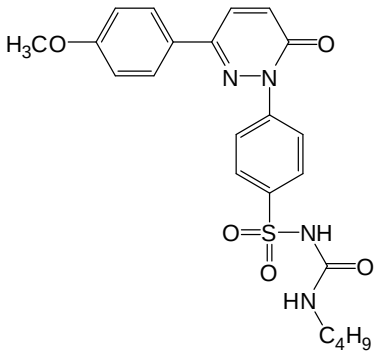
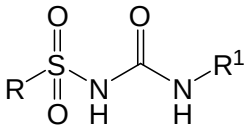


(53)

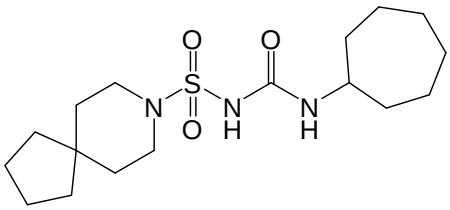


(54)

Wiseman *et al.,* 1965 have designed and synthesized a series of some novel substituted sulfonylureas **(55)**. Among them, compound **(56)** has been shown to have excellent oral bioavailability and has demonstrated good *in vivo* hypoglycemic activity in a rat model (Wiseman *et al.,* 1965).

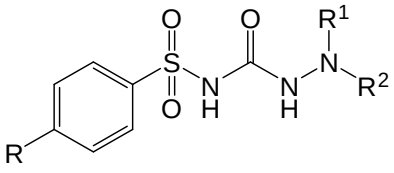


(55)

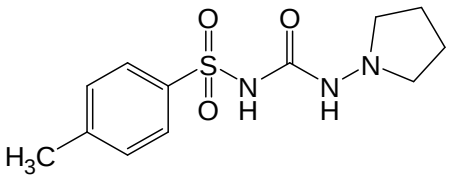


(56)

Wright *et al.,* 1962 reported the synthesis of a series of arylsulfonylsemicarbazides **(57)** and evaluated for their *in vivo* antidiabetic activity. From the results, it appears that cyclic amino derivatives such as **(58)**, **(59)**, **(60)**, **(61)**, **(62)** and **(63)** in general appear to be the most active derivatives (Wright *et al.,* 1962).



(57)



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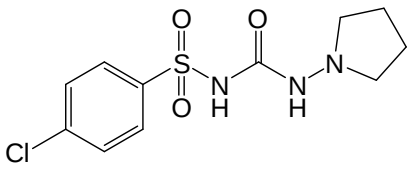
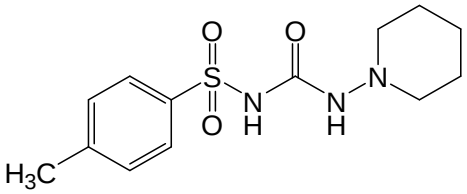


(59)



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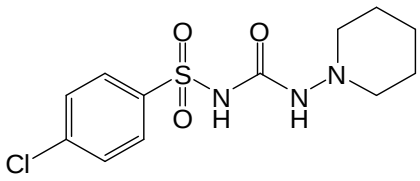
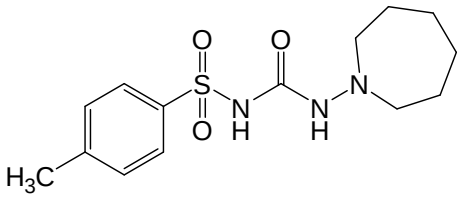
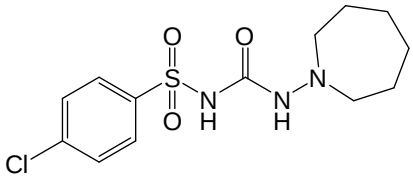


(61)

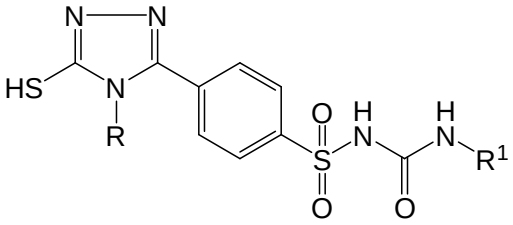


(62)



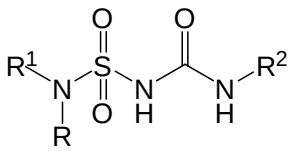
(63)

Mhasalkar *et al.,* 1971 have discovered a series of some new sulfonylurea derivatives of 4*H*-1,2,4-triazole **(64)** as potential hypoglycemic agents. Many compounds showed significant blood sugar lowering activity (Mhasalkar *et al.,* 1971).



(64)

McManus *et al.,* 1965 have reported the synthesis of some new substituted sulfonylureas **(65)**. The newly synthesized compounds have been evaluated for the antihyperglycemic activity in rats and among these compounds **(66)**, **(67)** and **(68)** showed significant antihyperglycemic activity in rat model (McManus *et al.,* 1965).



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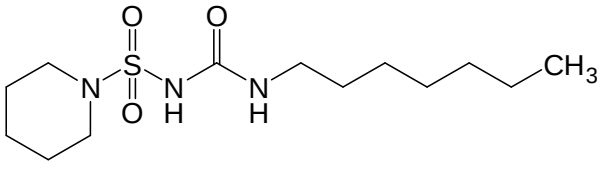

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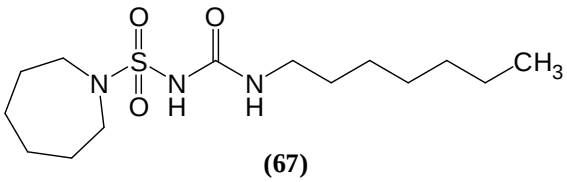

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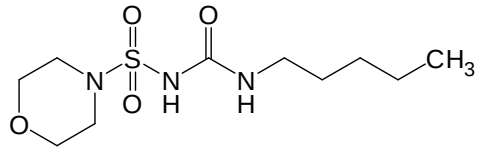
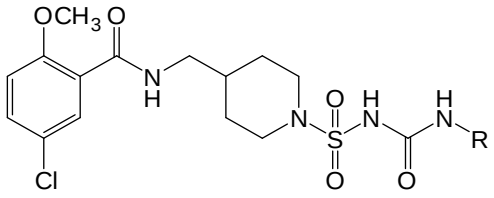
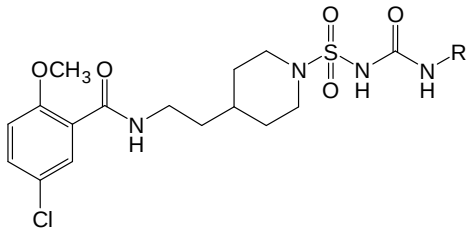


(68)

Sarges *et al.,* 1976 have been developed synthetic methods for a series of novel sulfonylurea derivatives **(69)**, **(70)**, **(71)** and **(72)**. The hypoglycemic activity of simple 1-piperidinosulfonylureas is greatly enhanced by attaching an acylaminoethyl function in the 4-position of the piperidine ring. Optimum activity is achieved when the acyl radical is 5-chloro-2-methoxybenzoyl, 2-methoxynicotinyl, 5-chloro-2-methoxynicotinyl, 1,2-dihydro-1-methyl-2-nicotinyl, 2,3-ethylenedioxybenzoyl, quinoline-8-carbonyl or 6-chloroquinoline-8-carbonyl. Optimal substituents on the terminal urea nitrogen are cyclohexyl, bicycloheptenylmethyl and in certain cases propyl, 7-oxabicycloheptanylmethyl and adamantly. One of these compounds **(73)** was found to be well tolerated in man and it displayed a very short plasma half-life (Sarges *et al.,* 1976).



(69)



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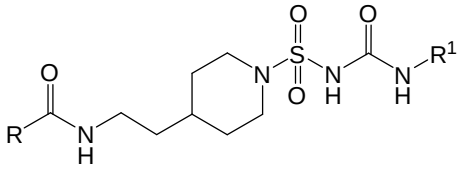

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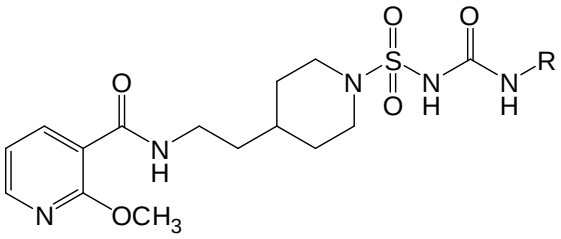
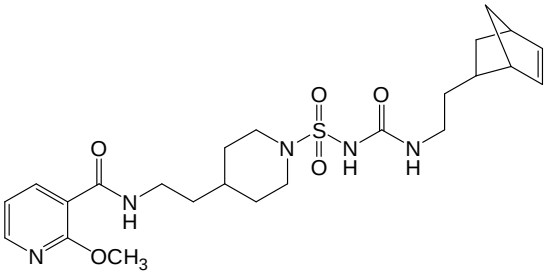
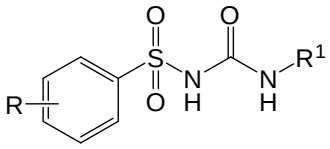


(72)

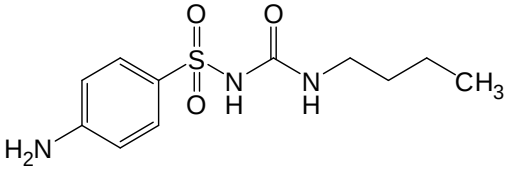


(73)

Hokfelt *et al.,* 1962 have prepared a series of 1-sulfonyl-3-alkylureas **(74)** and evaluated their blood glucose lowering activities. Among them the potential candidates are **(75)** and **(76)** which have potent blood glucose lowering activity (Hokfelt *et al.,* 1962).



(74)



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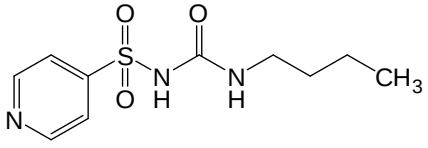
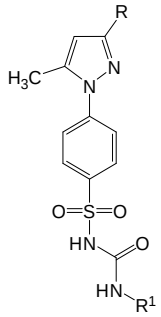


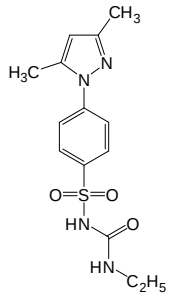
(76)

Soliman, 1979 have prepared a novel series of sulfonylurea derivatives of 3,5-disubstituted pyrazoles **(77)** for evaluation as hypoglycemic agents. Biological testing

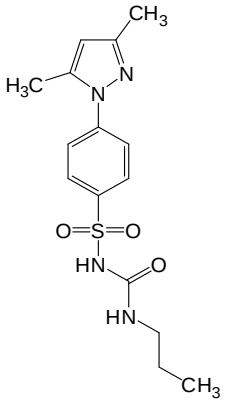
of these compounds showed that some **(78**, **79** and **80)** possessed significant antidiabetic activity (Soliman, 1979).



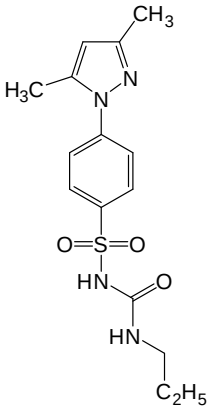
(77)



(78)

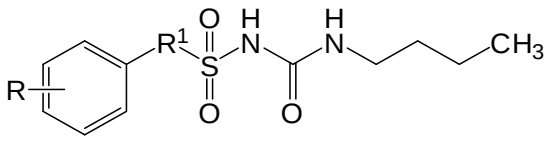


(79)

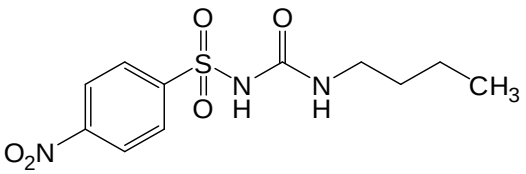


(80)

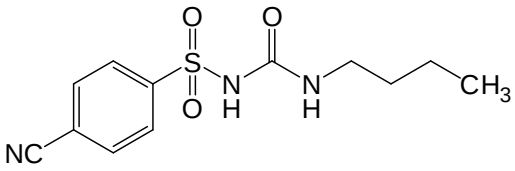
Loev *et al.*, 1963 have synthesized a series of sulfonylureas **(81)**. These compounds were screened for their hypoglycemic activity. Most of the compounds from this series exhibited good to moderate blood glucose lowering property. Compounds **(82)** and **(83)** have been found to exhibit significant hypoglycemic activity (Loev *et al.*, 1963).



(81)



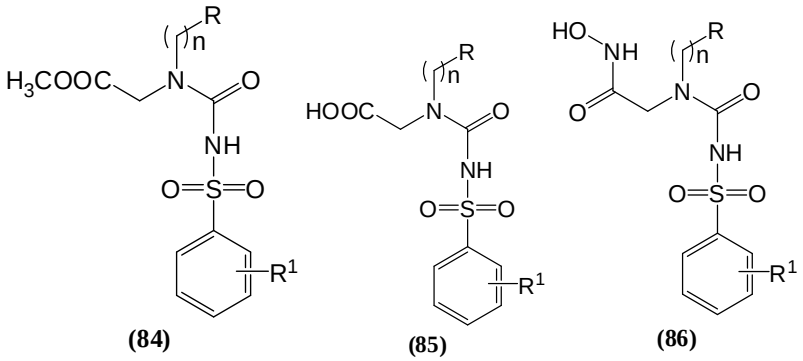
(82)



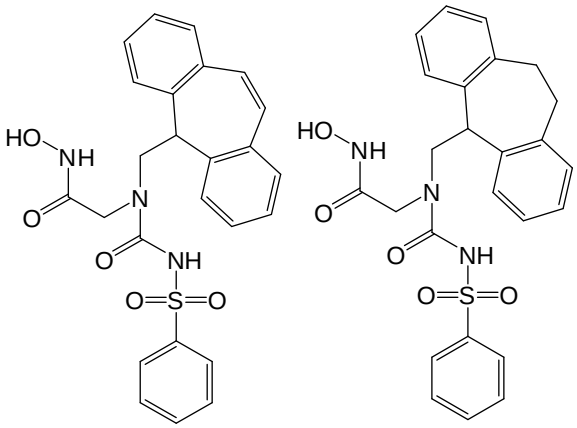
(83)

2.2.6 Antimicrobial Activity

Ilies *et al.*, 2003 have prepared a novel series of substituted sulfonylurea derivatives **(84)**, **(85)** and **(86)**. These new compounds were assayed as matrix metalloproteinase (MMP)/bacterial collagenase (ChC) inhibitors. Some of the new derivatives **(87)** and **(88)** reported here proved to be powerful inhibitors of the four MMPs such as MMP-1, MMP-2, MMP-8 and MMP-9 and of ChC, with activities in the low nanomolar series for a number of of the targeted enzymes, depend upon the substitution model at the sulfonylureido moiety and on the length of the spacer through which the dibenzosuberenyl/suberyl group is connected with the rest of the molecule. Several of these inhibitors also showed selectivity for the deep pocket enzymes (MMP-2, MMP-8 and MMP-9) over the shallow pocket ones MMP-1 and ChC (Ilies *et al.*, 2003).

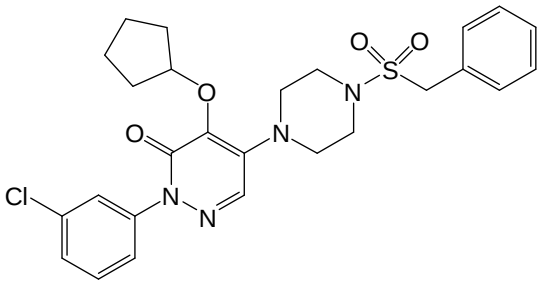


(84) **(85)** **(86)**



(87) **(88)**

Zych *et al.,* 2012 have discovered a series of sulfonylurea-based 1,3-β-D-glucan synthase inhibitors during a campaign for the Selection of the novel lead compounds **(89)** and **(90)**. While compounds of set **(91)** exhibit promising activity against medically appropriate fungal strains, efficiency against an *in vivo* systemic *C. albicans* infection type was not active (Zych *et al.,* 2012).



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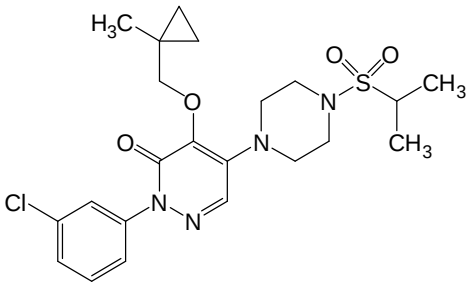

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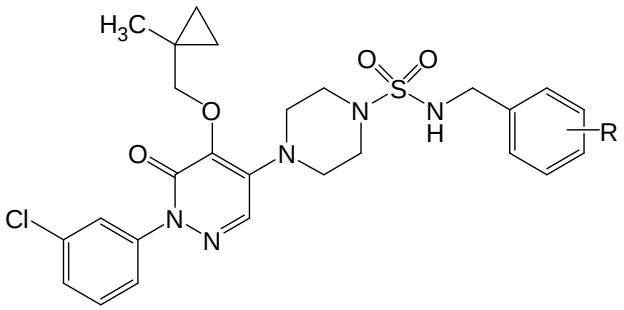
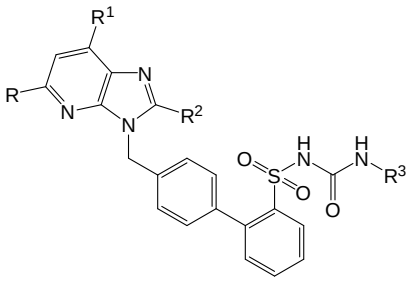


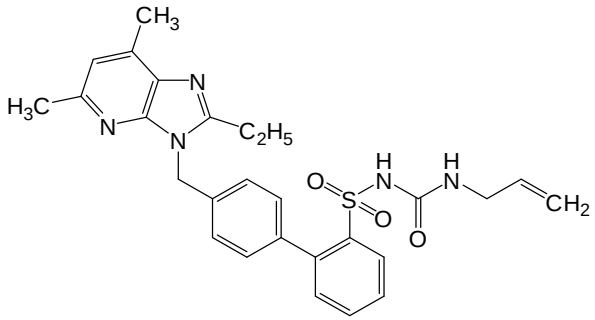
(91)

2.2.7 Angiotensin II (AII) Antagonists

Heitsch *et al.,* 1995 have designed and synthesized a series of new class of imidazo[4,5-b]pyridine biphenyl sulfonylureas **(92)**. All the synthesized compounds were evaluated for their AT_1 selective ANG II receptor antagonistic activity. Several members of this new class of antagonists efficiently inhibited the ANG II induced pressor response in pithed rats after intravenous (iv) and intraduodenal (id) administration. Consequently, the allyl-substituted sulfonylurea **(93)** was the most active antagonist exhibiting an IC_{50} value of 0.1 nM (Heitsch *et al.,* 1995).



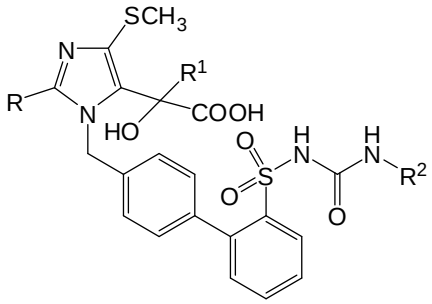
(92)



(93)

Deprez *et al.,* 1995a have prepared the synthesis of a set of 5α-hydroxyacid imidazolyl biphenyl sulfonylureas **(94)** and evaluated as potential angiotensin II (AII)

antagonists. This series was identified as potent and orally active compounds that bind with high affinity AT_2 receptor subtypes. All exhibited inhibitory activity with nanomolar affinity on both AT_1 and AT_2 receptors and with an AT_2/AT_1 ratio, lying in between 0.4 and 0.3. Compound **(95)** has been found to be exhibited significant antagonistic activity (Deprez *et al.,* 1995a).



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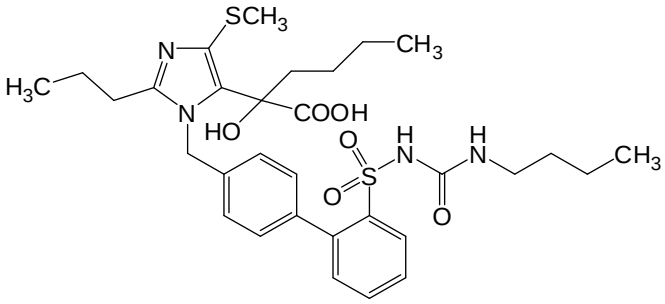
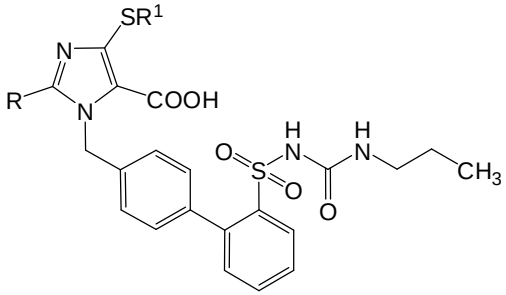
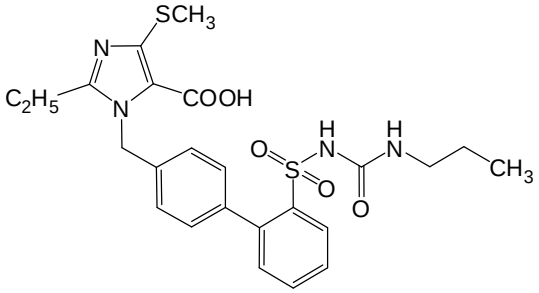


(95)

Deprez *et al.,* 1995b have prepared a novel series of highly potent orally active (imidazolylbiphenylyl) sulfonylureas **(96)** as new non-tetrazole angiotensin II (AII) receptor antagonists. Their activity was evaluated by AII receptor binding assay as well as by *in vivo* assays such as inhibition of the AII-induced pressor response in pithed rats. Most of the synthesized sulfonyl derivatives showed nanomolar affinity for the AT_1 receptor subtype. The *N*-propylsulfonylurea **(97)** as representative member of this series exhibited high oral activity in the pithed rat model with ID_{50} value of 0.38 mg/kg (Deprez *et al.,* 1995b).

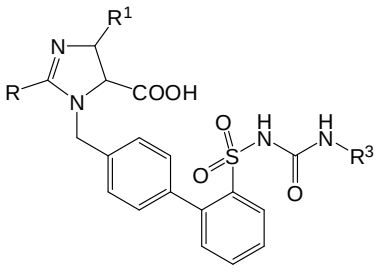


(96)



(97)

Deprez *et al.,* 1995c have synthesized a series of some novel imidazolyl biphenyl sulfonylureas **(98)** and evaluated as potential angiotensin II (AII) antagonists. This series was identified as potent and orally active compounds that bind with high affinity both to the AT_1 and AT_2 receptor subtypes. The high *in vitro* potency on both receptor subtypes as well as the oral activity of compound **(99)**, associated with its structural analogy with the AT_1 selective HR 720, make it useful tool for discovering the advantages of balanced compounds over AT_1 selective antagonists (Deprez *et al.,* 1995c).



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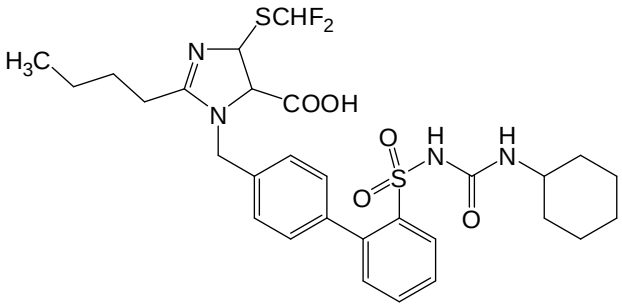
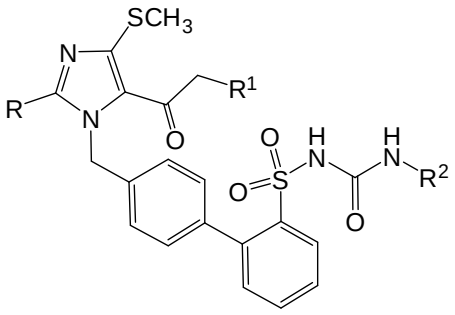
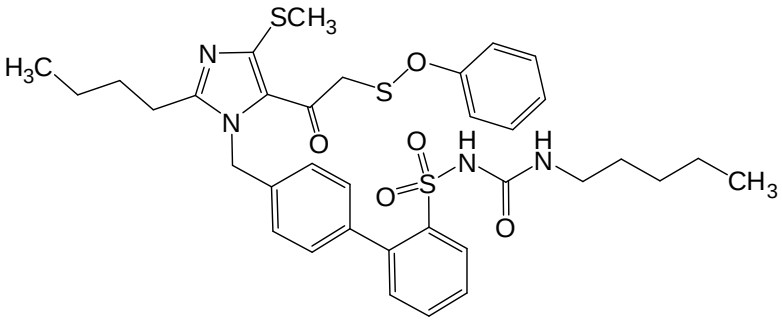


(99)

Deprez *et al.,* 1995d have synthesized a series of some novel imidazoles bearing sulfonylurea moiety **(100)** and evaluated as potential angiotensin II (AII) antagonists. Compound **(101)** is a potent AII inhibitor that binds with nanomolar affinity to both AT_1 and AT_2 receptor subtypes. *In vivo*, this compound inhibited pressor response induced by AII (0.75 µg/kg) in pithed rats, at low doses (0.04 mg/kg i.v. and 0.8 mg/kg p.o.). It may therefore be beneficial in the treatment of hypertension (Deprez *et al.,* 1995d).



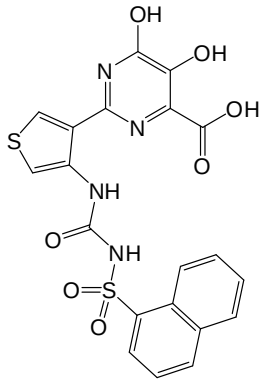
(100)



(101)

2.2.8 Antiviral Activity

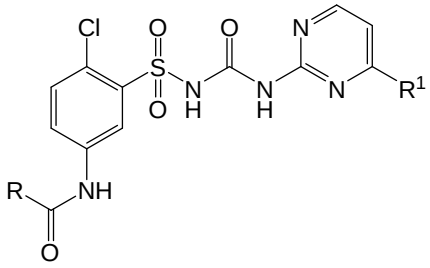
Pacini *et al.,* 2009 have prepared the set of synthesized sulfonylurea derivative **(1)** as potential inhibitor of hepatitis C virus (HCV) NS5B RdRp (Pacini *et al.,* 2009).



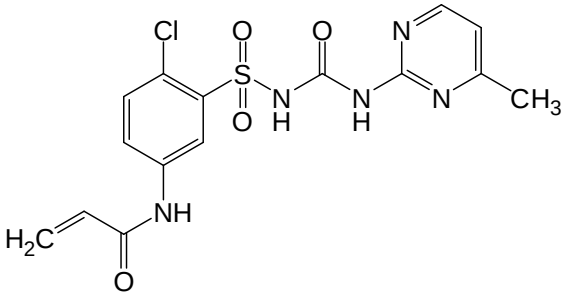
(102)

2.2.9 Antitubercular Activity

Pan *et al.,* 2012 have prepared the synthesis of a set of some novel monosubstituted sulfonylurea derivatives **(103)**. These compounds were evaluated against *Mycobacterium tuberculosis* H37Rv *in vitro*. The results showed compounds **(104)**, **(105)** and **(106)** exhibited moderate antitubercular activities with MIC values in the range of 20-100 mg/L. Compounds **(107)** and **(108)** displayed good antitubercular activities (MIC 10 mg/L), which were comparable with that of the sulfometuron methyl. Both of the two compounds showed little cytotoxicities, with an IC_{50} against THP-1 cells greater than 100 mg/L (Pan *et al.,* 2012).



(103)



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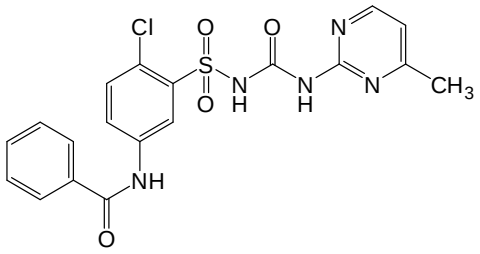

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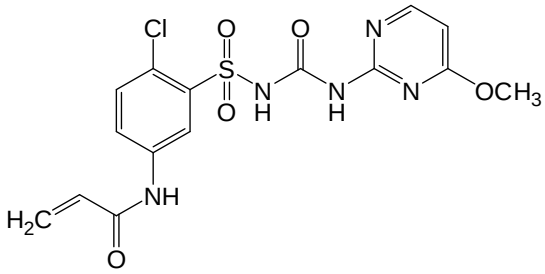
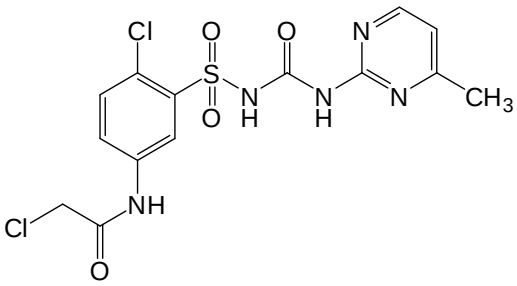
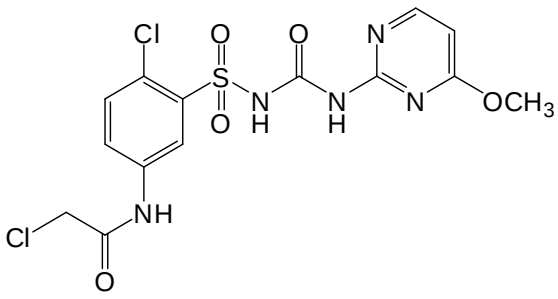


(106)



(107)

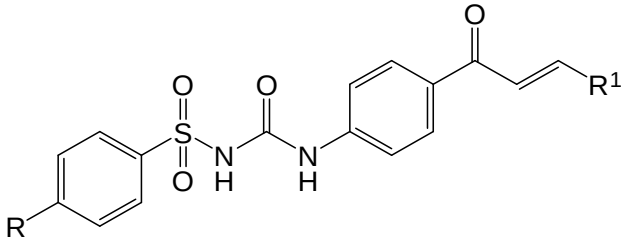


(108)

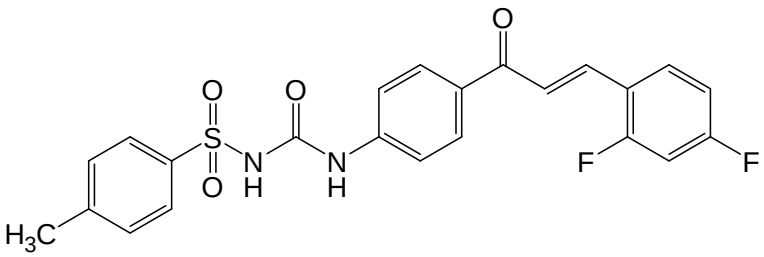
2.2.10 Antimalarial Activity

Leon *et al.,* 2007 have prepared a novel set of sulfonylurea derivatives **(109)** and examined their antimalarial activity, include inhibition of *in vitro* hemoglobin hydrolysis, *in vitro* enlargement of a chloroquine-resistant strain of *Plasmodium falciparum*,development of *Plasmodium berghei* in murine and malaria hemozoin formation. The most dynamic antimalarial compound was (*E*)-1-[4′-(3-(2,4-difluorophenyl)acryloyl)phenyl]-3-tosylurea **(110)** with values of IC_{50} of 1.2 µM

against cultured *Plasmodium falciparum* parasites. Biological consequences propose a reasonable effective antimalarial activity for this compound, but also involve that its activity may begin from an unidentified mechanism. Certainly, these type of compounds could act against malarial parasites through multi mechanisms (Leon *et al.*, 2007).



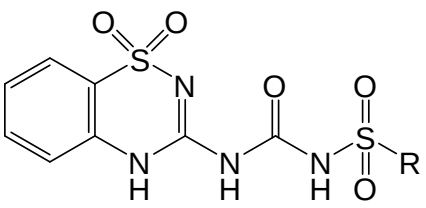
(109)



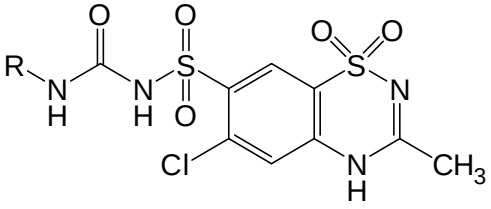
(110)

2.2.11 Potassium Channel Modulator

Khelili *et al.*, 1995 have synthesized a series of some new 3- and 7-sulfonylurea-1,2,4-benzothiadiazin-1,1-dioxide derivatives **(111** and **112)** and evaluated as potassium channel modulators. Various sulfonylurea moieties were introduced on position 3 and 7 of the heterocycle without, or by means of methylene and phenyl spacers. On the rat aortic rings, several compounds displayed vasodilating activities, especially compound **(113)**, which was more active than cromakalim and diazoxide at low doses (0.1 µM) and more active than diazoxide between 1 and 10 µM (Khelili *et al.*, 1995).



(111)



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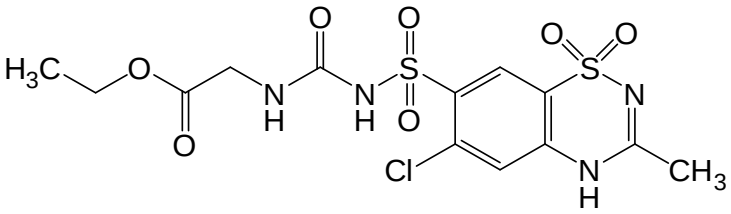
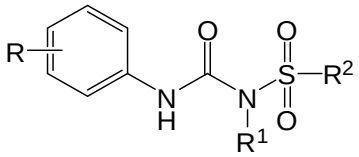


(113)

2.2.12 Hypocholesterolemic Activity

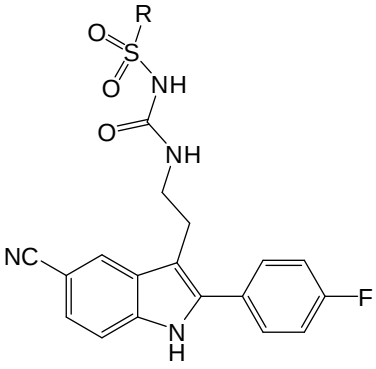
Roth *et al.,* 1995 have prepared a novel series of substituted sulfonylureas **(114)** examined for the ability to inhibit the enzyme acyl-CoA, cholesterol acyltransferase (ACAT) *in vitro* and lower plasma cholesterol in cholesterol-fed rats *in vivo.* Although compounds from this series were generally weak inhibitors of ACAT *in vitro*, several displayed excellent hypocholesterolemic activity *in vivo (*Roth *et al.,* 1995).



(114)

2.2.13 Chemokine Antagonists

Winters *et al.,* 2008 have prepared a series of sulfonylurea bioisosteres of carboxylic acids **(115)** and evaluated as chemokine receptor (CXCR2) antagonists. Of these, compound **(116)**, has been shown to have excellent oral bioavailability and has demonstrated good activity *in vivo* in a rat model of lung injury (Winters *et al.,* 2008).



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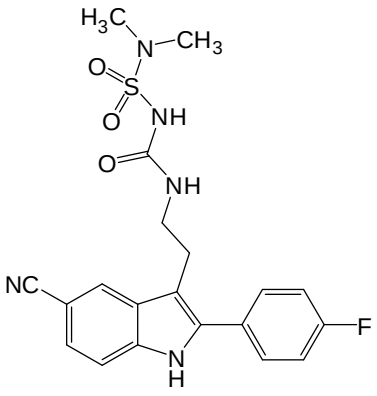
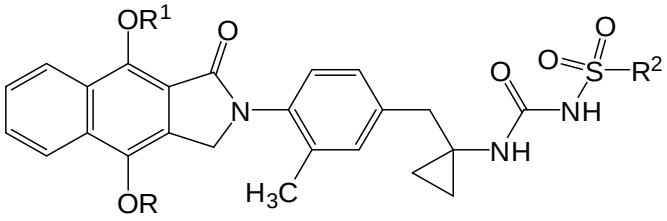


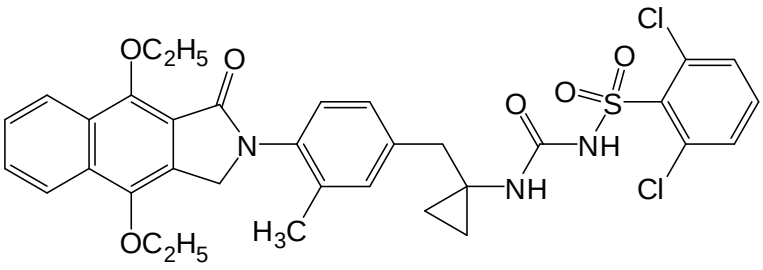
(116)

2.2.14 Prostaglandin Antagonists

Burch *et al.*, 2011 have synthesized a series of some novel sulfonylureas **(117)** and evaluated for selective prostaglandin E_2 (PGE_2) subtype EP_4 receptor antagonistic activity. These compounds showed subnanomolar inherent binding activity towards to the EP_4 receptor, and tremendous selection towards another prostanoid receptors (EP_1, EP_2 and EP_3) with fine pharmacokinetic structure. MF-592 **(118)**, the optimized compound from the sulfonylurea chain, has a essential on the entire preclinical profile signifying that it is appropriate for advance development (Burch *et al.*, 2011).



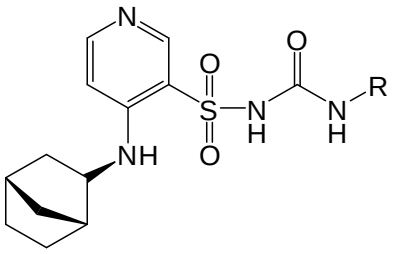
(117)



(118)

2.2.15 Human Bombesin Receptor Agonists

Lo *et al.*, 2011 have designed and synthesized a series of substituted sulfonylureas **(119)** and evaluated for their agonistic activity against human bombesin receptor subtype-3 (BRS-3). Compound **(120)**, which has nanomolar potency, selectivity for human BRS-3 versus the other bombesin-like receptors, and good bioavailability (Lo *et al.*, 2011).



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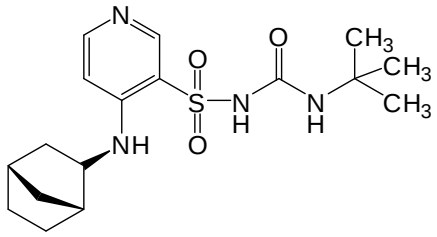
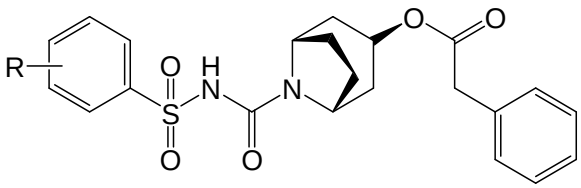


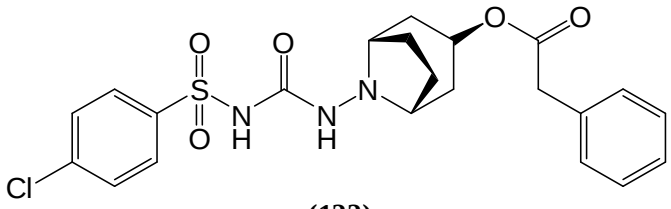
(120)

2.2.16 Human Steroid Sulfatase Inhibitors

Nussbaumer *et al., 2003* have synthesized a series of some new nortropinyl-arylsulfonylureas **(121)** and evaluated as reversible inhibitors of human steroid sulfatase (STS). Among them, compound **(122)** was identified as a hit from high-throughput screening. A series of analogues was prepared in order to explore the essential structural elements for STS inhibition, and structure–activity relationships were established. Mechanistic investigations revealed that the compounds are reversible, competitive inhibitors of STS (Nussbaumer et al., 2003).



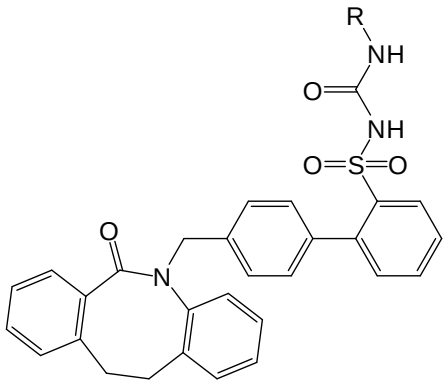
(121)



(122)

2.2.17 Prostaglandin Antagonists

Ruel *et al., 1999* have synthesized a series of some novel sulfonylureas **(123)** and evaluated as selective prostaglandin E_2 (PGE_2) subtype EP_1 receptor antagonists. These compounds showed nanomolar fundamental binding activity towards the EP_1 receptor, and good selection towards additional prostanoid receptors (EP_2, EP_3 and EP_4) with fine pharmacokinetic profile. The optimized compound **(124)** from the sulfonylurea derivative, was originated for future scope (Ruel et al., 1999).



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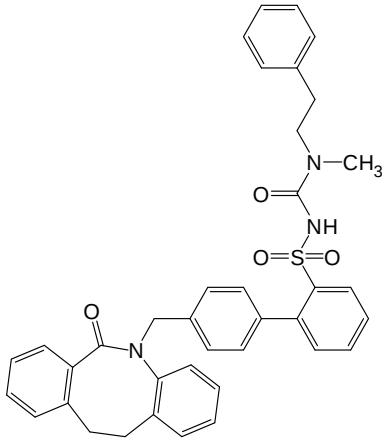
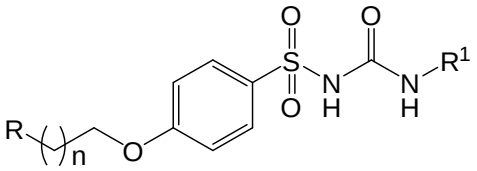


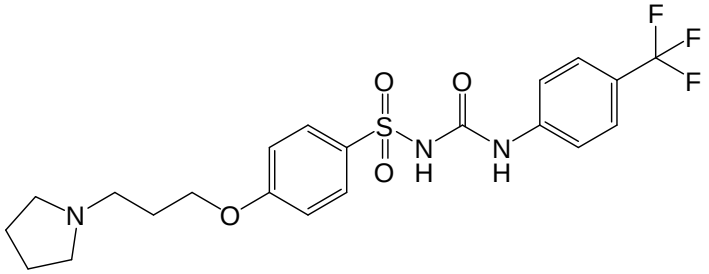
(124)

2.2.18 Histamine-H_3 Antagonists

Ceras *et al.,* 2012 have prepared to design and synthesis a new set of non-imidazole derivatives, basis on a fundamental amine ring associated through an alkyl spacer of changeable extent to a phenoxysulfonylurea moiety **(125)**. These type of compounds were primarily tested for histamine h_3 enzyme binding affinities, signifying that a propoxy chain linkage between the amine and core ring might be necessary for selective binding affinity. Compound **(126)**, 1-(naphthalen-1-yl)-3-[(*p*-(3-pyrrolidin-1-ylpropoxy) benzene)] sulfonylurea showed the finest H_3 antagonism affinity. Though, ever since all these type of derivatives unsuccessful to obstruct K_{ATP} channels, the linkage of these two interrelated moieties should not be a good pharmacophore for obtaining novel double H_3 antagonists with insulinotropic activities, signifying the requirement to suggest a new compound hybrid prototype (Ceras *et al.*, 2012).



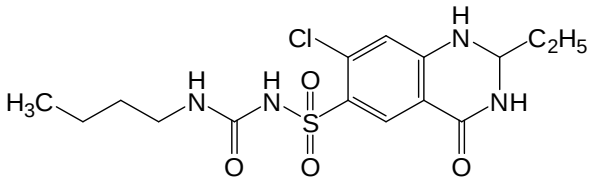
(125)



(126)

2.2.19 Diuretic

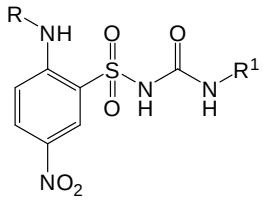
Ceras et al., 2012 have reported the 1,2,4-benzothiadiazine based sulfonylurea **(127)** as potential diuretic (Ceras et al., 2012).



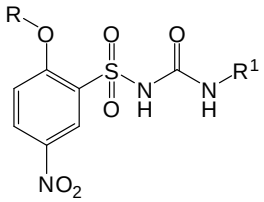
(127)

2.2.20 Human Thromboxane Antagonists

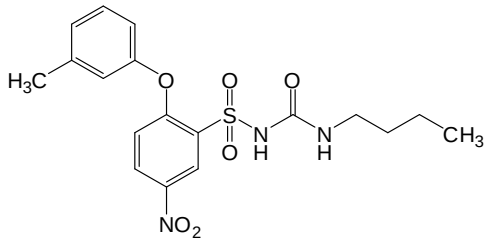
Hanson *et al.,* 2007 have designed and synthesized a series of some new nitro-substituted benzenesulfonylurea derivatives **(128)** and **(129)**. These compounds screened as selective antagonists of the TPα and TPβ isoforms of the human thromboxane A_2 receptor. The SAR studies was calculated based upon the outcome of a functional assay, TP-mediated intracellular calcium ($[Ca^{2+}]_i$) mobilization participated on the two part isoforms. Selective nature and point of various structural moieties was distinct for mutually activity and selectivity toward TPα and TPβ isoforms. 3 compounds **(130**, **131** and **132)**, showed increased selectivity for TPβ relative to TPα (18.1:1, 19.9:1, 23.2:1 respectively), were chosen for future tests, and their activity was definite in a Thrombocyte aggregation test (Hanson *et al.,* 2007).



(128)



(129)



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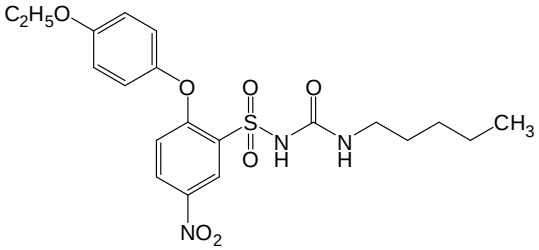
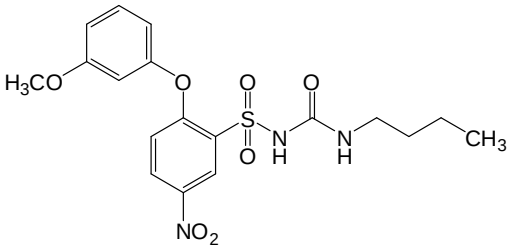
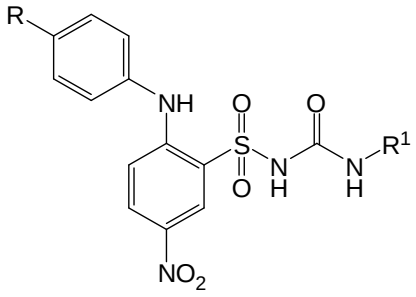


(131)

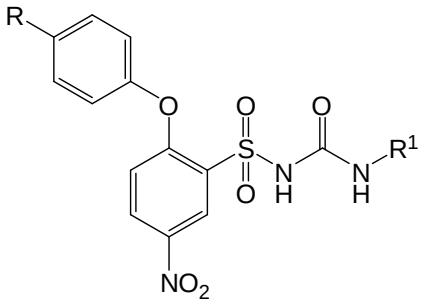


(132)

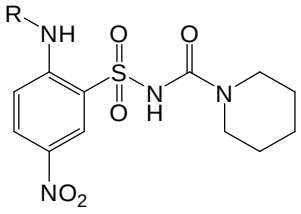
Hanson *et al.,* 2006 have synthesized and evaluated a series of some novel nitro-substituted benzenesulfonylurea derivatives **(133)**, **(134)** and **(135)** designed as antagonists of the human thromboxane receptor TP/TXA2 receptors. Since there are two TP isoforms in humans, the development of selective compounds for TPα and/or TPβ is clearly of great clinical interest for human diseases. Hence, they have studied the affinity and activity of these compounds on both TPα and TPβ. All compounds evaluated, exhibited very high affinity for both TP receptors, mainly acting in the nanomolar range. Finally, the most promising compounds **(136)** and **(137)** were evaluated on platelet aggregation and confirmed their potent TP receptor antagonism useful as antiplatelet agents (Hanson *et al.,* 2006).



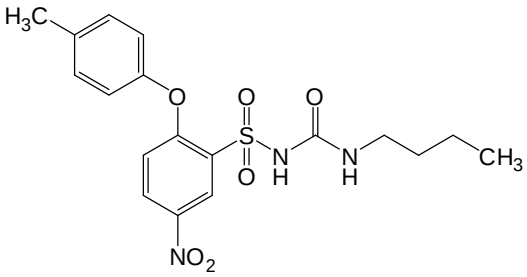
(133)



(134)



(135)



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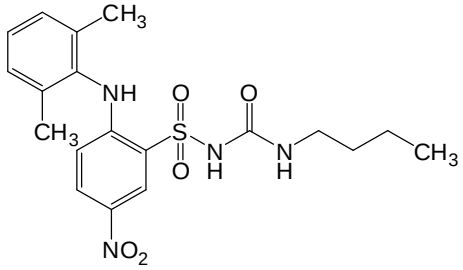


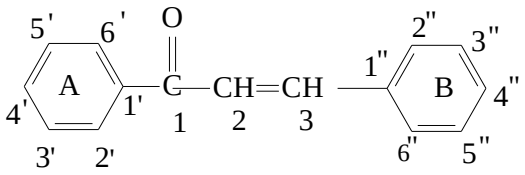
(137)

2.3 CHALCONES

Chalcones **(1)** are generic compounds that belongs to the flavonoid family and bearing the 1,3-diphenyl-2-propen-1-one framework (Maayan et al., 2005; Nowakowska, 2007; Go et al., 2005). They are open-chain flavonoids with two ringed aromatic

chains that are joined by a 3 carbonα,β-unsaturated carbonyl system. Chalcones are profusely present in nature mostly in ferns to higher plants (Mark and Nagarathnam, 1991) and mostly have polyhydroxylated in the aryl rings. In plants, most of the chalcones are transformed to the corresponding (2S)-flavanones that are stereo-specifically catalyzed by the enzyme chalcone isomerase. The close biogenetic and structural relationship between flavanones and chalcones explains co-occurrence as natural products.

2.3.1 General Structure of Chalcone



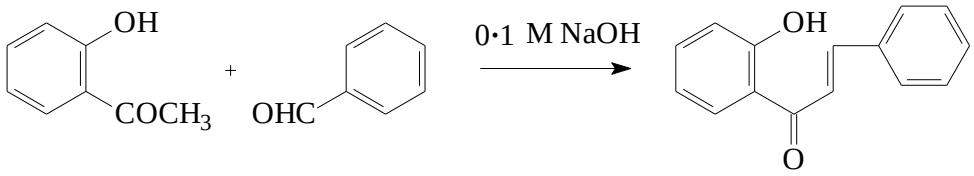
(1)

All chalcones provide pink coloration mostly with concentrated H_2SO_4 (positive Wilson test) and when a phenolic OH- group is present; they provide violet coloration when present with alcoholic $fecl_2$ solution (Wilson, 1938).

2.3.2 Methods of Synthesis of Chalcones

Chalcones can be attained by the base or acid catalyzed by aldol condensation of acetophenones with aromatic aldehydes (Claisen and Claparede, 1981; Datta et al., 1971; Makrandi and Kumar, 2008).

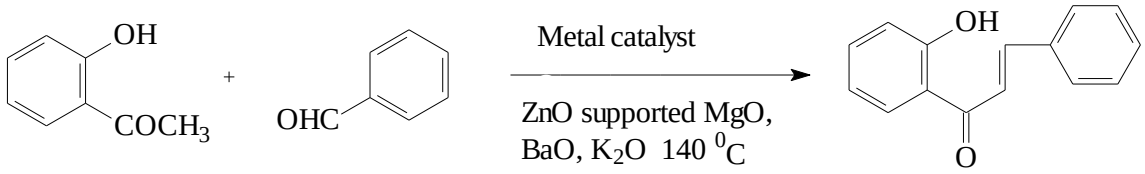
1. Benzaldehyde reacts with 2'-hydroxyacetophenone in the presence of 0.1 Molar NaOH gives the chalcone (Reichel and Muller, 1941) (**Scheme 2.7**).



Scheme 2.7

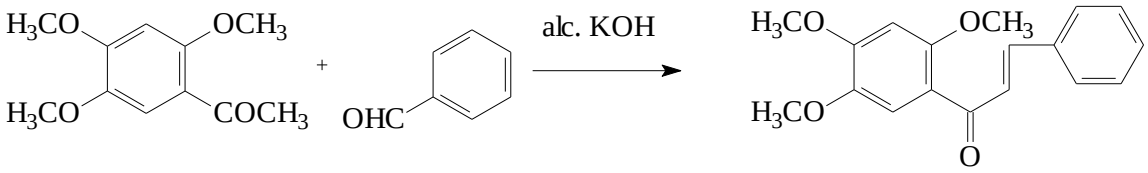
2. Liquid stage Claisen–Schmidt condensation between benzaldehyde and 2'-hydroxyacetophenone was conducted over a ZnO_2 carried metal oxide catalyst

under solvent free circumstances to obtain 2'-hydroxychalcone (Saravanamurugan et al., 2005) (**Scheme 2.8**).



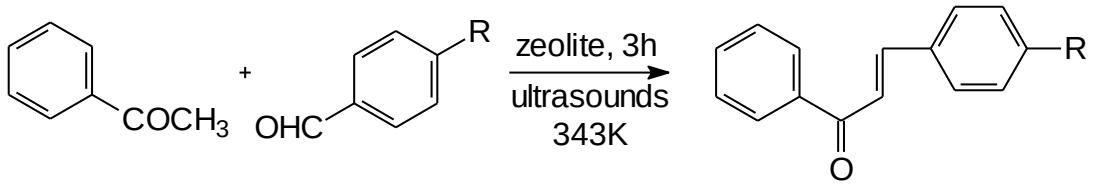
Scheme 2.8

3. The condensed 2',4',5'-trimethoxyacetophenone with equimolar proportions of aromatic aldehydes in presence of 30% alcoholic alkali (at room temperature) to yield chalcones (Anjaneyulu et al., 1994) (**Scheme 2.9**).



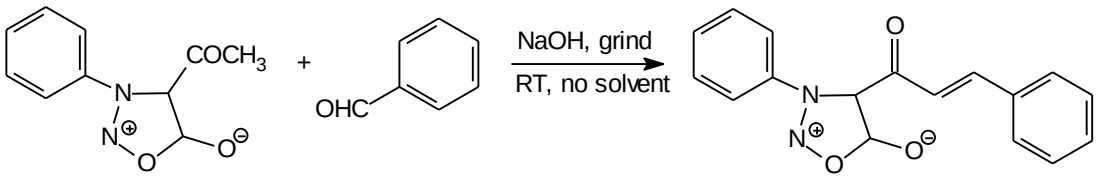
Scheme 2.9

Condensation of Claisen-Schmidt between acetophenone and benzaldehyde by sonochemical and heat stimulate reactions as zeolite as catalyst beneath solvent free condition provides chalcone (Elizabeth et al., 2006) (**Scheme 2.10**).



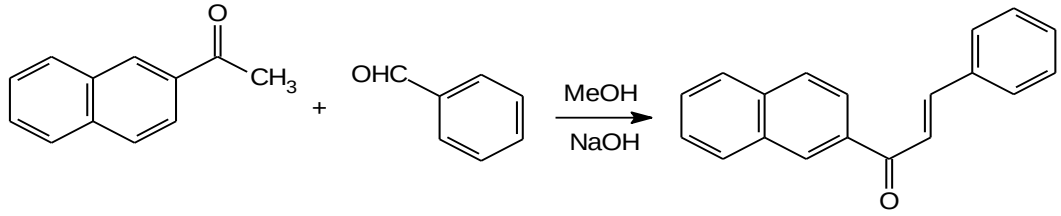
Scheme 2.10

4. 4-Acetyl-3-aryl-syndones are focused in different arylaldehydes in existence through a base catalyst beneath to the solvent free condition which are to be yield in syndonechalcones (Bala and Ganesha, 2003) (**Scheme 2.11**).



Scheme 2.11

5. 2-naphthylmethylketones is substituted with arylaldehydes in the occurrence of sodium hydroxide under Meoh as Reagent gave the subsequent chalcones (Deshpande et al., 1999) (**Scheme 2.12**).

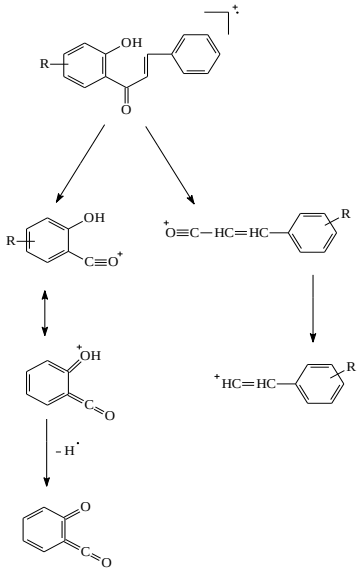


Scheme 2.12

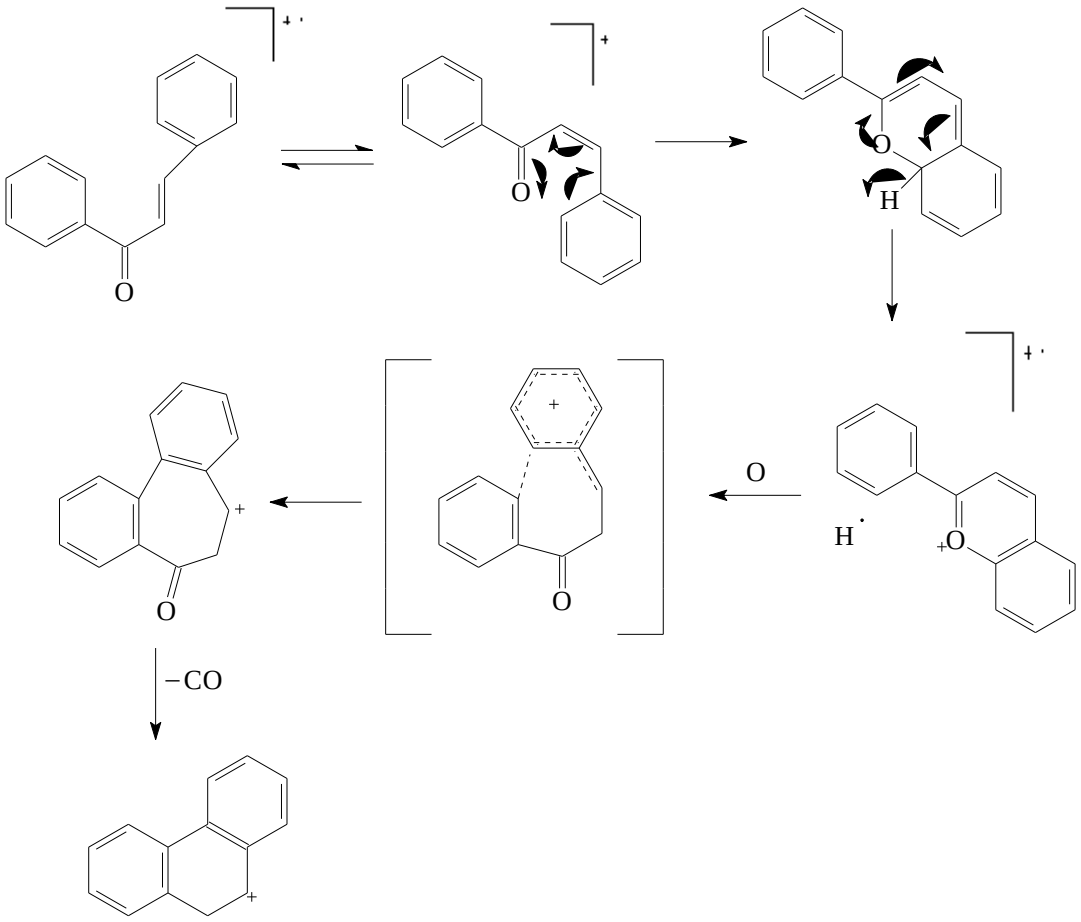
2.3.3 Proximity impact of Chalcones

Chalcones conjointly bring about to the weird fragment particle [M-H]+ involving a kind of unit aromatic substitution reaction by the elimination of AN ortho substitutent from an aromatic ring with additional cyclization. This ends up in the formation of a extremely stabilised benzopyrylium ion (Van et al., 1972) (**Scheme 2.14**) and this kind of fragmentation is usually called proximity impact. The ion thus undergoes structural rearrangements, which allows fragmentation pathways that will eventually result in loss of CO (Ardanaz et al., 1998; Ronayne et al., 1966; Ardana et al., 1991).

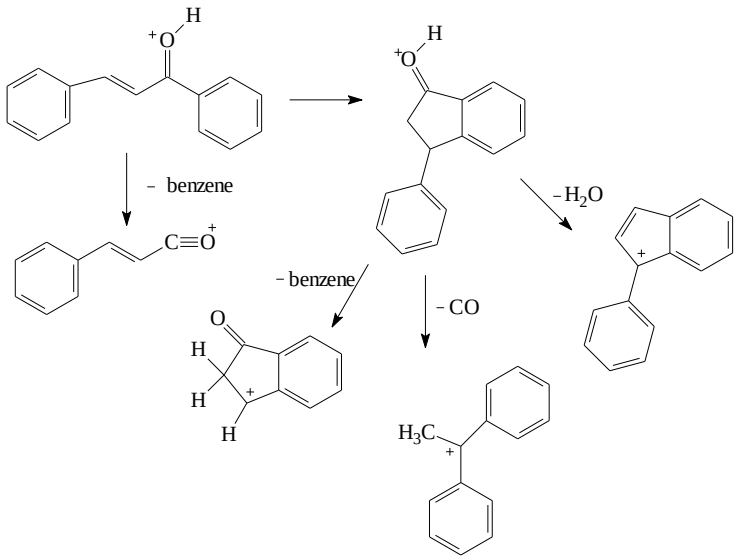
Protonated chalcones produced by electrospray ionization through MS/MS conducted experiment were identified to form three vital fragment ions due to loss of water, CO and benzene (Tai et al., 2006) (**Scheme 2.15**).



Scheme 2.13. Typical fragmentation pattern of a 2'-Hydroxychalcone.



Scheme 2.14. Mechanism of formation of $[M-H]^+$ and loss of CO from $[M-H]^+$ ion of chalcone



Scheme 2.15. Fragmentation of $[M+H]^+$ ion of chalcone

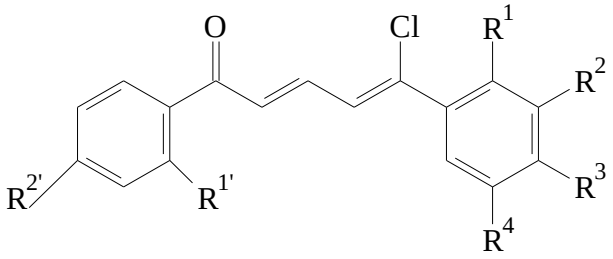
2.3.4 Therapeutic Potential of Chalcones

Chalcone is associated with various biological activities (Geiger and Conn, 1945; Ambedkar et al., 1961).

Chalcone has biological and pharmacological activities (Dhar, 1981), including anti-inflammatory, analgesic, antitumor, antimicrobial, cytotoxic, antitubercular, antioxidant, antiviral, anti-HIV, antiulcerative, antileishmanial, antihistaminic, anticonvulsant, antiprotozoal, antimalarial, immunomodulatory, antihyperglycemic, antihyperlipidemic, antifedent, and antiplatelet activities.

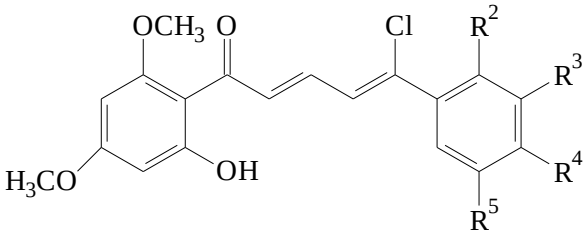
2.3.5 Antimicrobial activity

The antimicrobial activity of chalcones (2) is being gradually recognized by Bandgar and Gawande, 2010.



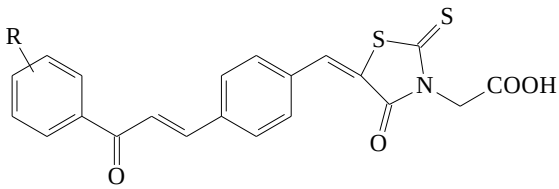
(2)

Bandgar *et al*., 2010 also reported in another study that the chalcones **(3)** showing antibacterial and antifungal activities.



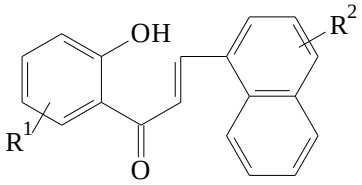
(3)

Chen *et al*., **2010** synthesized new chalcones **(4)** showing antibacterial activity



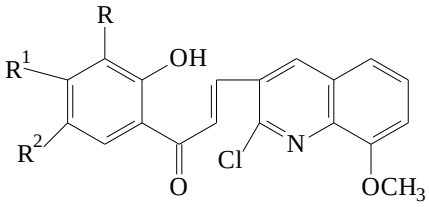
(4)

Vibhute *et al*., 2010a reported the synthesis of some new chalcones containing inhibition against *E.coli* **(5)**.



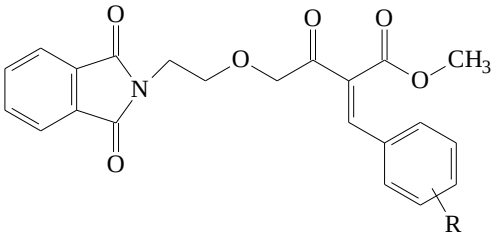
(5)

Vibhute *et al*., 2010b also synthesized novel chalcones with 2-chloro-8-methoxyquinolinyl moiety showing antibacterial activity **(6)**



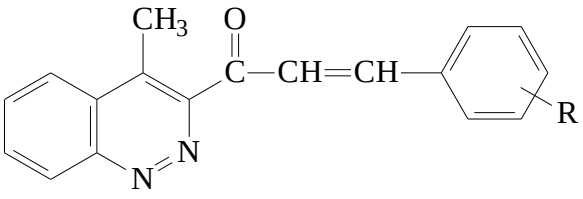
(6)

Rathod *et al*., 2010 prepared novel chalcones with phthalimidoester exhibited good antimicrobial activity **(7).**



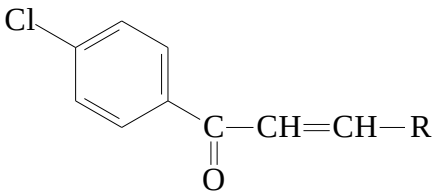
(7)

Gautam *et al*., 2010 reported some new cinnoline based chalcones showing antimicrobial activity **(8).**



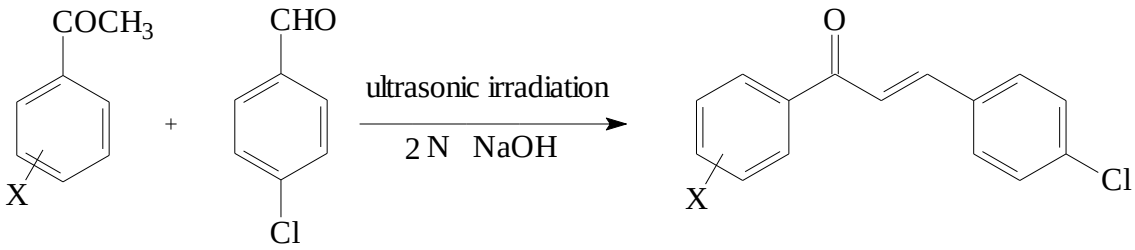
(8)

Paramesh *et al*., 2010 reported synthesis of some new chlorine containing chalcones possessing antimicrobial activity **(9)**.



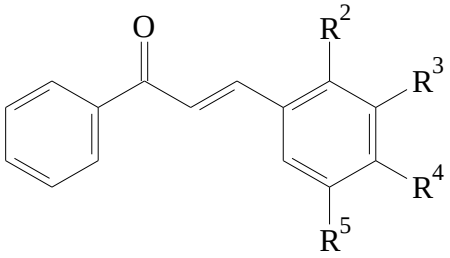
(9)

Guptha *et al*., 2010 reported synthesis of chalcones using ultrasonic irradiation **(10)** for antimicrobial and antifungal activities.



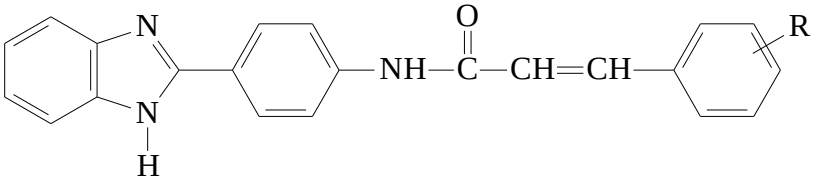
(10)

Batovska *et al*., 2009 reported large series of novel chalcones possessed 4'-chloro or 3',4',5'-trimethoxy groups for antibacterial activity **(11).**



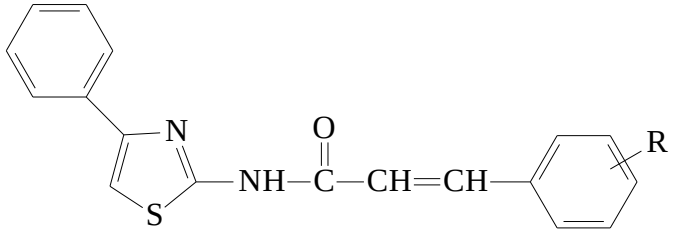
(11)

Baviskar *et al*., 2008 synthesized new benzimidazolylchalcones **(12)** bearing phenyl, 3-fluorophenyl, 3-bromophenyl and 4-methoxyphenyl, 4-hydroxyphenyl moieties showing antifungal and antibacterial activities.



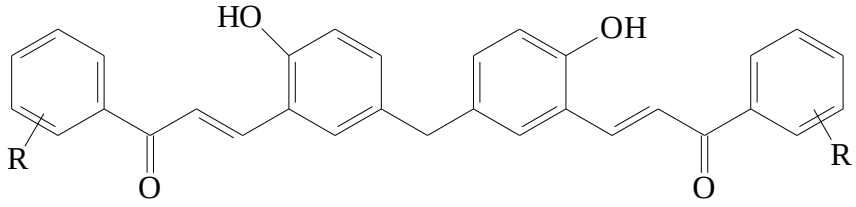
(12)

Baviskar *et al*., 2009 also synthesized new thiazolylchalcones **(13)** showing antimicrobial activity.



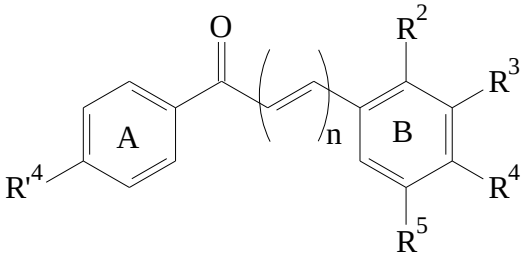
(13)

Reddy and Nagaraj, 2008 was synthesized novel bis-chalcones **(14)** that are showing antibacterial and antifungal activities.



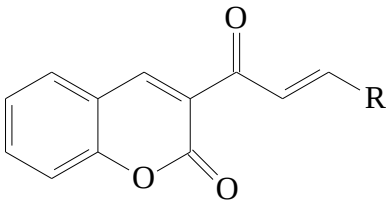
(14)

Lahtchev *et al*., 2008 reported synthesis of active chalcones possessed phenyl, 3-hydroxyphenyl, 3-hydroxy-4-methoxyphenyl and 4-hydroxyphenyl moieties and showing antifungal activity **(15)**.

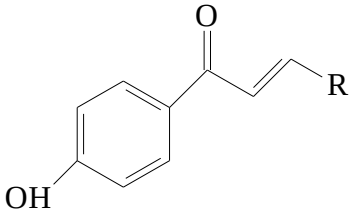


(15)

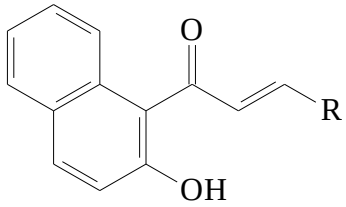
Prasad *et al*., 2008 carried out QSAR analysis of synthesized chalcone derivatives **(16, 17** and **18)** showing antibacterial activity.



(16)

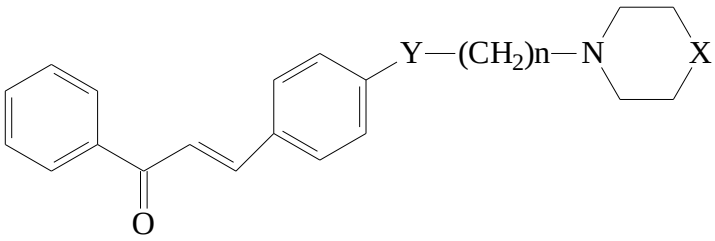


(17)



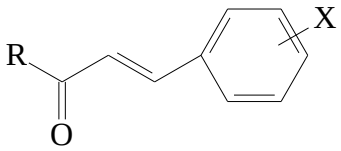
(18)

Nowakowska *et al*., 2008 synthesized antibacterial and antifungal compounds with a series of substituted chalcones **(19).**

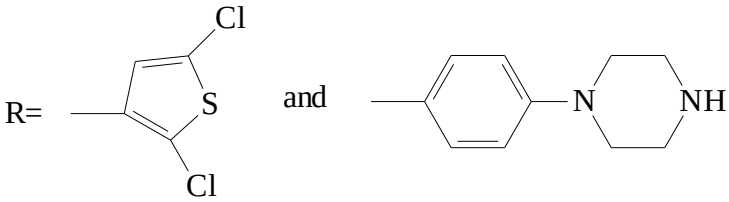


(19)

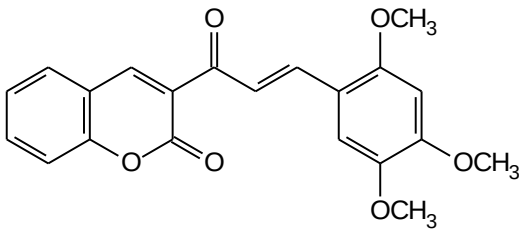
Tomar *et al*., 2007 synthesized new chalcones containing piperazine or 2,4-dichlorothiophene moiety **(20)** showing antimicrobial activity.



(20)

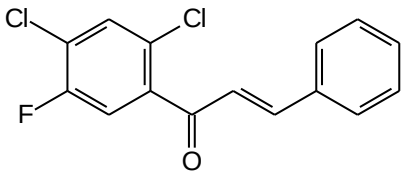


Prasad et al., 2007 was synthesized 3-[1-oxo-3-(2,4,5-trimethoxyphenyl)-2-propenyl]-2H-1-benzopyran-2-ones **(21)** showing antimicrobial activity.



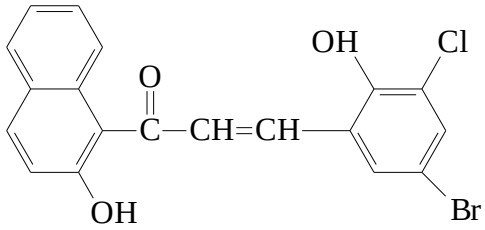
(21)

Karthikeyan *et al., 2007* was synthesized 3-aryl-1-(2,4-dichloro-5-fluorophenyl)-2-propen-1-ones **(22)** performing antimicrobial activity.



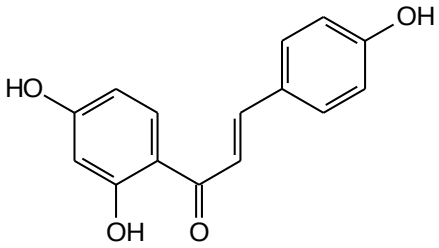
(22)

Prasad *et al*., 2006 synthesized a naphthalene moiety chalcone **(23)** having antifungal activity.



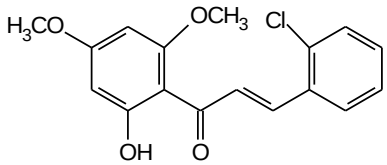
(23)

Machodo *et al*., 2005 synthesized isoliquiritigenine **(24)** showing antibacterial activity.



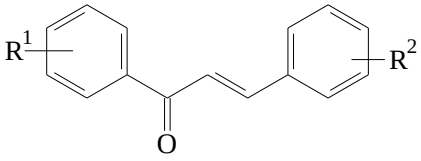
(24)

Boeck *et al*., 2005 was synthesized new xanthoxylin-derived chalcones **(25)** exhibited antifungal activity.



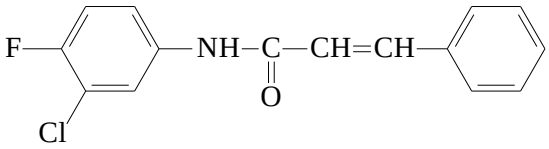
(25)

Nielsen *et al*., 2004 synthesized bioisosteric replacement of the 4' –hydroxy group in some new chalcones **(26)** showed significant antibacterial activity.



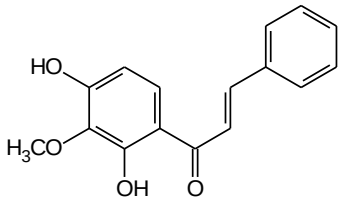
(26)

Rao *et al*., 2004 isolated chlorine and fluorine substitution chalcones having **(27)**, antimicrobial activity.



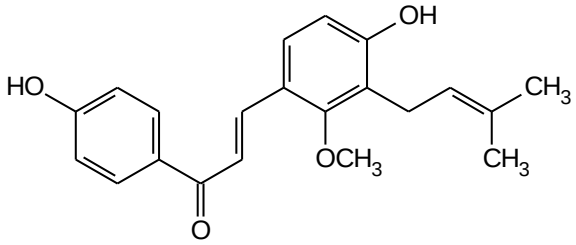
(27)

Stevaz *et al., 2004* synthesized a 2',4'-dihydroxy-3'-methoxychalcone **(28)** having antifungal activity.



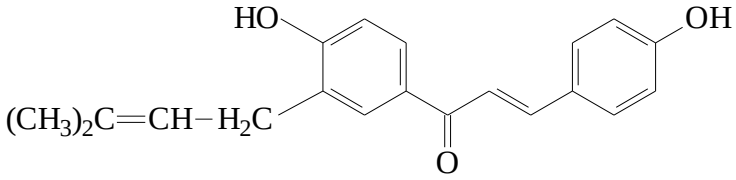
(28)

Tsukiyama *et al., 2002* was synthesized a licochalcone C, a retrochalcone **(29)** showed significant antibacterial activity.



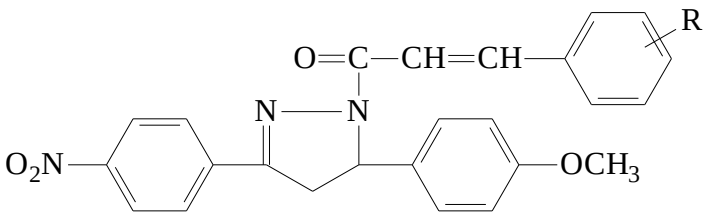
(29)

Sohly *et al., 2001* synthesized prenylated chalcones **(30)** shows antifungal activity.



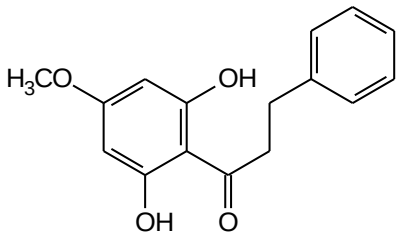
(30)

Desai *et al*., 2003 synthesized some new substituted pyrazoline moiety chalcones having **(31)** antibacterial activity.



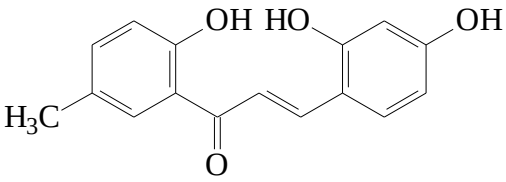
(31)

Okunade *et al., 1997* isolated a dihydrochalcone **(32)** which showed antibacterial activity.



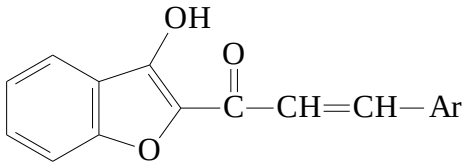
(32)

Tsuchiya *et al., 1994* was isolated a hydroxychalcone **(33)** that showed antifungal activity.



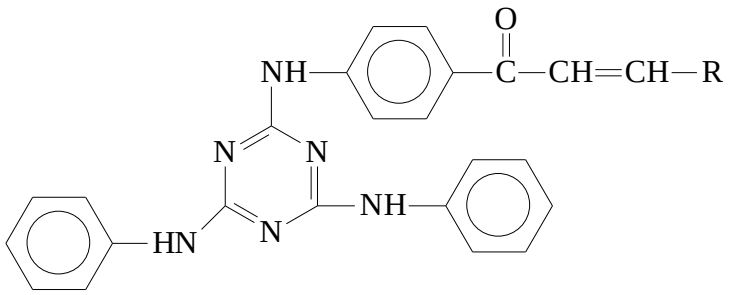
(33)

Swamy and Agasimundin, 2010 synthesized some new benzofuran moiety chalcones having **(34)** antimicrobial activity.



(34)

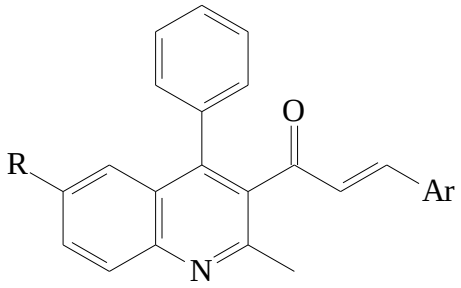
Some novel S-triazine based chalcones (Solankee et al., 2010) by the reaction of 2,4-bis-(phenylamino)-6-(4'-acetylphenylamino)-s-triazine with various aldehydes form chalcones **(35)** showing antibacterial activity.



(35)

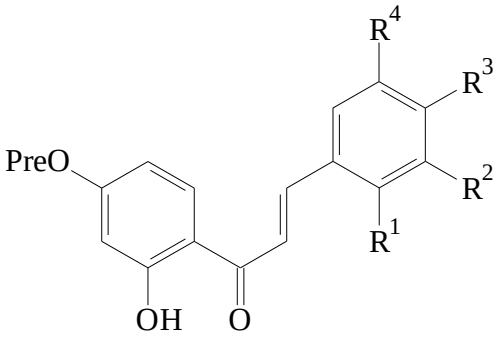
2.3.6 Anti-inflammatory activity

Kotra *et al*., 2010 synthesized a new series of quinolinyl chalcones **(36)** showing anti-inflammatory activity by carrageenan-induced acute paw edema method in rats.

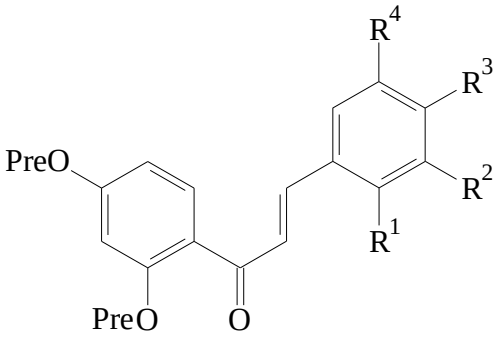


(36)

Reddy *et al*., 2010 synthesized new mono and di-O-prenylated chalcone derivatives **(37** and **38)** showing inflammatory activity.

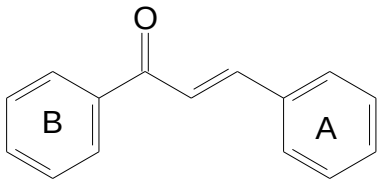


37 (a-e)



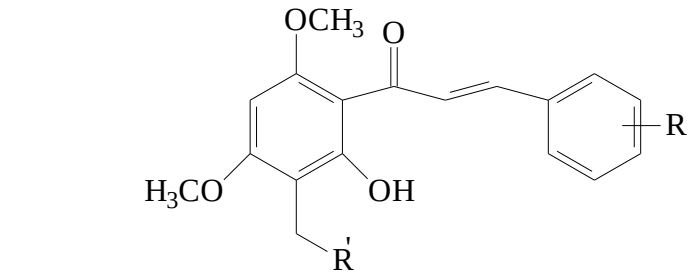
38 (a-e)

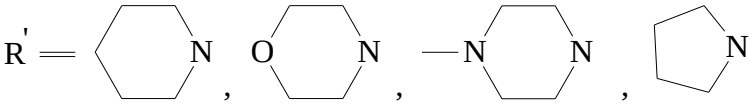
Bandgar *et al*., 2010a synthesized some methoxychalcones **(39)** and were screened for their anti-inflammatory activities.



(39)

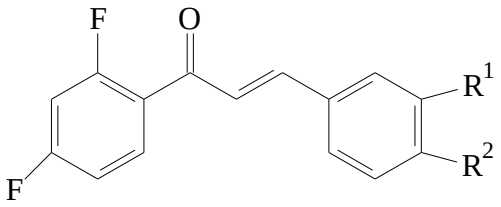
Bandgar *et al*., 2010b synthesized new nitrogen containing chalcones **(40)** screened for anti-inflammatory activities.





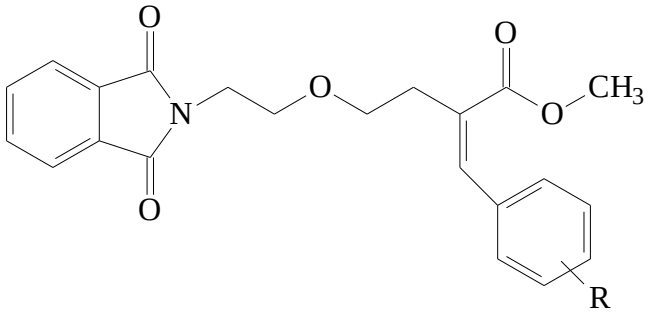
(40)

More and Ramaa, 2010 synthesized novel series of five 1-(2',4'-difluorophenyl)-3-(substituted phenyl)-1,3-propanediones **(41)** shown good anti-inflammatory activity.



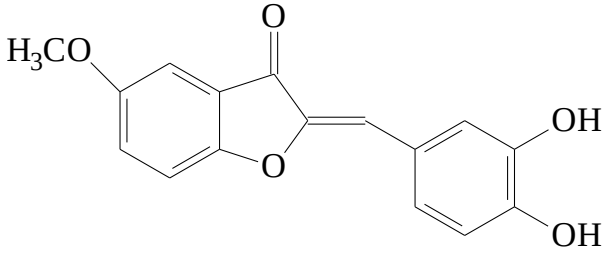
(41)

Gaikwad *et al*., 2010 synthesized new chalcones of phthalimidoester **(42)** possessing good anti-inflammatory activity.



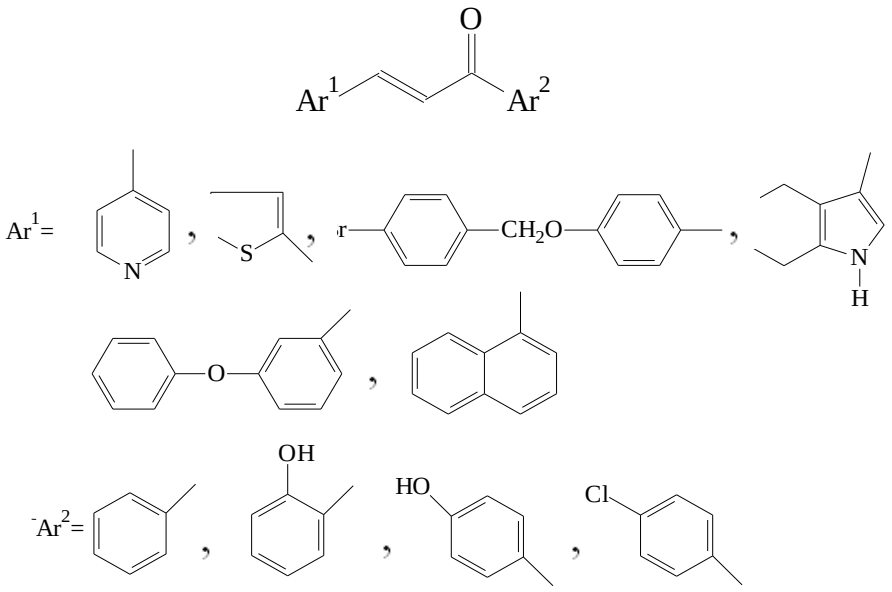
(42)

Heidari *et al*., 2009 synthesized a new rigid benzofuran-3,4-dihyroxychalcone **(43)** possessing anti-inflammatory effects.



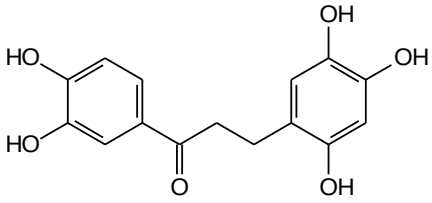
(43)

Maria *et al*., 2008 synthesized a series of chalcones **(44)** possessed high inhibitory activity on lipid peroxidation.



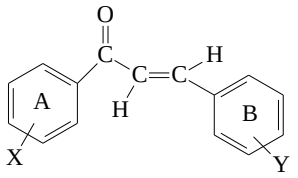
(44)

Ito *et al., 2007* synthesized a reduced chalcone **(45)** having COX-2 activity.



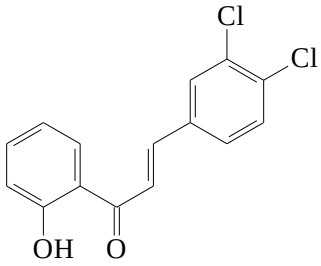
(45)

Okunrobo *et al*., 2006 synthesized some chalcones **(46)** possessing anti-inflammatory activity using carrageenan-induced rat paw edema assay.



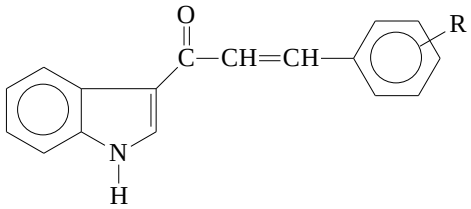
(46)

Shen *et al., 2005* isolated a 2'-hydroxy-3,4-dichlorochalcone **(47)** showed cancer activity and anti-inflammatory.



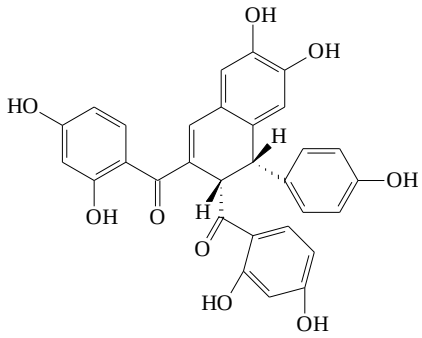
(47)

Rani *et al*., 2004 synthesized chalcones of indole **(48)** showing anti-inflammatory activity against carrageenan-induced edema in albino rats.

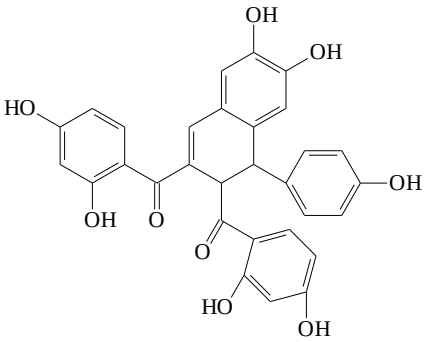


(48)

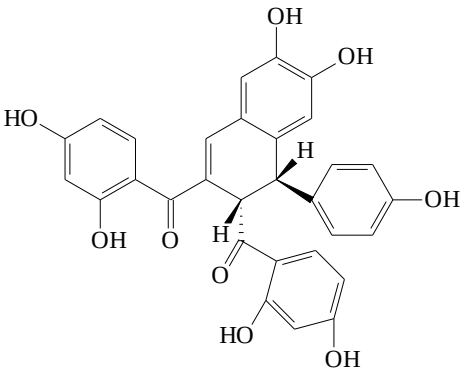
Viana *et al*., 2003 conducted anti-inflammatory activity from a fraction containing three dimeric chalcones **(49**, **50** and **51)**.



(49)

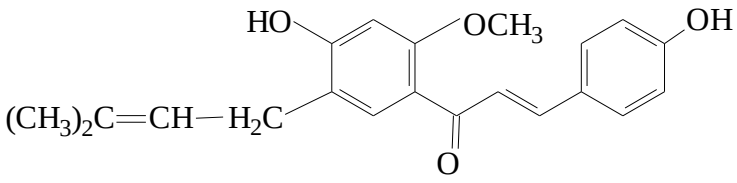


(50)



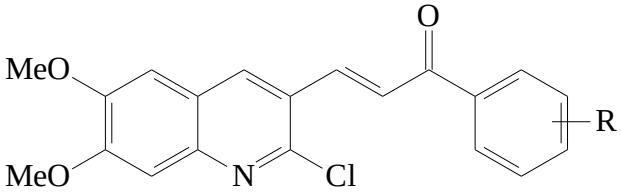
(51)

Zhao *et al., 2003* synthesized dihydroxanthohumol **(52)** shows anti-inflammatory activity.



(52)

Herencia *et al*., 1998 synthesized chalcones are showing anti-inflammatory activity.



(53)

Hence, there is a need to design, deveop and synthesize novel Diarylsulfonylurea-chalcone compounds that show anti-inflammatory properties that can efficiently control diseases.