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Synthesis and molecular modeling studies of some new derivatives of benzylidene-2-phenyl-1H-imidazol-5(4H)-one

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Abstract

Imidazole derivatives have been synthesized widely as cyclooxygenase inhibitors. In the following research synthesis of ten benzylidene-2-phenyl-1H-imidazol-5(4H)-one derivative **(2.1-2.10)** was carried out, as selective COX-2 inhibitors, using the principle of Erlenmeyer-Ploch synthesis. In a two step synthesis the compounds were synthesized in high yield using microwave as an alternate source of energy. The structures of synthesized imidazole derivatives were proved by means of their IR, ^{1}H-NMR and mass spectral analysis. The compounds were then analyzed using *in silico* docking and toxicity studies, for various parameters like hydrophobicity, hydrogen bonding, sitemap interactions, oncogenicity, teratogenicity and immunotoxicity. Among the synthesized compounds, **2.1, 2.2, 2.3, 2.8 and 2.10** exhibited significant glide score as an analgesic using 5COX as receptor and compounds **2.4, 2.5** exhibited maximum predictable toxicity.

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Keywords

COX, anti-inflammatory, benzylidene, imidazolone

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAID'S) are the main therapeutic agents for the treatment of Rheumatoid arthritis. It is understood that these drugs act by inhibition of enzyme cycloxygenase (COX) [1, 2]. Although these drugs are used globally, they are associated with one of the major side effects of GIT-ulceration[3]. The existing therapy of NSAIDs is non-selective towards COX-2 inhibitors, which therefore gave rise to a new class of anti-inflammatory agents, in the form of coxibs (Celecoxib, Rofecoxib etc.), having selective activity towards COX-2 enzyme. Unfortunately, Rofecoxib was banned due to the thromboembolic adverse effect it produced. Lot of research is being done since then for the development of new agents which can lessen the sensation of pain, especially chronic pain, which is still undertreated. The following study is indented for the same.

Rationale

A large number of research studies aimed at finding selective COX-2 inhibitors have

been reported[4-7]. Many of these have synthesized using CADD techniques to develop a new COX-2 inhibitor containing oxazoles, pyrazoles and imidazoles as core moiety[8-14]. In a Fujita-Ban modified *de Novo* approach, three series of diaryl heterocycles namely, diaryl imidazoles[15] diarylpyrazoles[16] and diaryloxazolones[17] were studied and it was inferred from the studies that diarylimidazoles posses better selective activity towards COX-2. Therefore, it was essential to synthesize some new derivatives of diarylimidazoles and study those using computational techniques before performing related pharmacological studies.

Chemistry

Synthesis of oxazolone involves the condensation of aromatic aldehydes and hippuric acid with a stoichiometric amount of fused sodium acetate in the presence of acetic anhydride; as the dehydrating agent, this reaction is known as the Erlenmeyer Plöchl reaction. The method involves preparation of azlactones (oxazolones) in a Z configuration (originally assigned to the E configuration) by condensation of aromatic aldehyde with hippuric acid in the presence of acetic anhydride[18]. It is observed that aldehyde condenses under the influence of a base with reactive methylene group in the azlactone which is formed by the dehydration of benzoylglycine, when the latter reacts with acetic anhydride in the presence of sodium acetate [19, 20]. Synthesis of substituted imidazoles (**2.1-2.10**) was carried out according to Scheme-1. The reaction proceeds when lone pair of nitrogen attacks carbonyl carbon. Upon restoration of carbonyl group as amide, the oxadiazole ring breaks and the oxygen accepts a proton from the reaction mixture. The hydroxyl was removed as water with closure of ring to form and imidazole. The imidazoles were characterized on the basis of IR, NMR and Mass spectral analysis

MATERIALS AND METHODS

Synthesis

All melting points were determined by open capillary tube method and are uncorrected. I. R.- spectra were recorded on Perkin-Elmer-Spectrum RX-IFTIR spectrophotometer. ^{1}H-NMR spectra were recorded on Avance II (Bruker) (400 MHz) spectrometer in DMSO using TMS as internal standard and chemical shifts are indicated in δ (ppm). Mass Spectra were recorded using Waters Micromass Q-Tof Micro which is hybrid quadrupole time of flight mass spectrometer equipped with ESI. Chemicals were purchased from commercial suppliers and were used without any further purification.

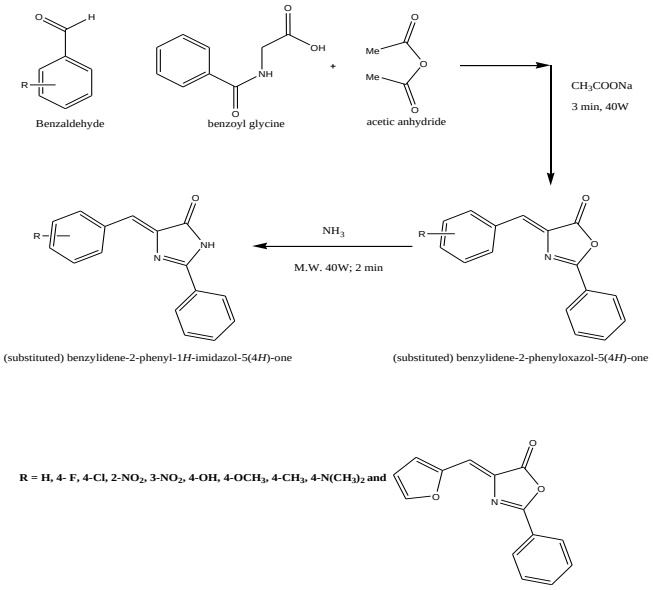
Step-1

Equimolar quantities of hippuric acid (2 g, 0.011 mol), redistilled benzaldehyde (0.011 mol) and acetic anhydride (1.12 g, 0.011 mol) were mixed together in a conical flask. To the above mixture anhydrous sodium acetate (2 g) was added and the flask was heated under microwave irradiation at 40W for 40-50 seconds. The liquefied mixture was then cooled, stirred well and heated again for 30 seconds at intervals, for a total of 3 minutes. Ethanol (q.s.) was then added to the above mixture in the conical flask and the mixture was then allowed to stand overnight. The crystalline product so obtained was filtered at suction and washed with boiling water and dried. The product was then recrystallized with benzene.

Step-2

Compound obtained in Step-1, substitutedbenzylidene-2-phenyloxazol-5(4H)-one (1g) was taken an Erlenmeyer flask and mixed with excess strong ammonia solution (10 ml) and rectified spirit (q.s.). The mixture was then irradiated in microwave for a total of 2 minutes at 50W with 30 sec interval in between each pulse. The mixture was then concentrated on a hot plate and left overnight. The crystals obtained were collected the following day as pure product. As the by-product obtained in the reaction is only water the product was not purified further.

The reaction scheme is shown as scheme-1.

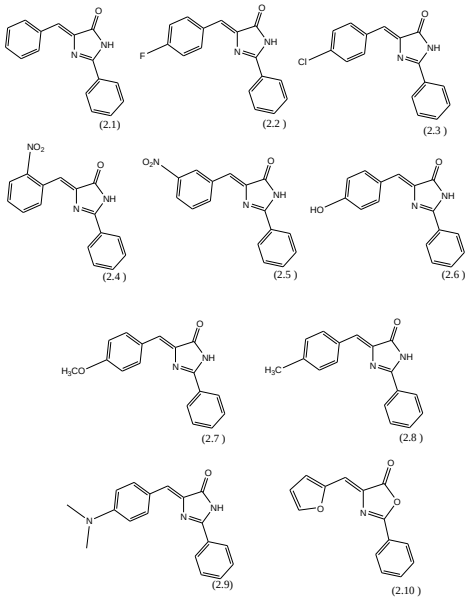


In silico molecular docking studies and toxicity prediction

Molecular docking studies were carried out using Suite 2012: Maestro, version 9.3, Schrödinger, LLC, New York, NY, 2012. The enzyme cycloxygenase, obtained from protein data bank was used as a receptor (ID: 5COX). Ligand preparation was done using LigPrep, version 2.5, Schrödinger, LLC, New York, NY, 2012. Docking studies were carried out using Glide, version 5.8, Schrödinger, LLC, New York, NY, 2012. The toxicity of the compounds were predicted by computational method using Pallas version 3.7.1.2 Hazard Expert prediction software and pentium IV processor (Pallas, 2006). For docking

studies the energy minimized ligands were docked at the selected grid of the receptor having X, Y, Z scale at 60.3312, 44.6724 and 76.0573 Aº, respectively. For toxicity studies structures were drawn and run using and Hazard Expert form Pallas to obtain values for various parameters like toxicity oncogenicity, teratogenicity, membrane-irritation etc. were obtained on a scale of 100.

Structures of the synthesized compounds



Results and Discussion

The IR spectra of the synthesized compounds revealed bands for different functional groups *viz.* aromatic, olefinic and ketonic. In compounds (1.1- 1.10) the presence of aromatic ring was confirmed by the presence of weak bands between 3045-3100 cm^{-1} due to aromatic C-H str. The olefinic double bond in conjugation with the aromatic ring as well as keto appears between 3090-3010 cm^{-1}. The important band which confirms the formation of azlactone ring is the band for ketonic functional group. It is effect of unsaturation which increases the frequency of carbonyl absorption band. The azlactone ring is a type β-γ type lactone ring; a five membered (γ) lactone ring with double bond at β to carbonyl functional group or α to –O- , for which an intense carbonyl absorption band is obtained between1790-1800 cm^{-1}. Lastly, the band for C=N str is obtained between 1689-1471 cm^{-1}, confirming the formation of oxazole ring. Physical data and spectral results for individual compounds are given in Table 1.

Stereochemistry

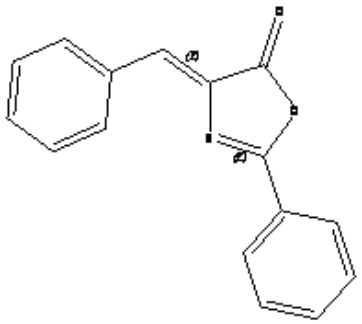
It was discussed previously that the compounds are obtained in Z configuration. It can be visualized that both the high priority groups in the synthesized compounds lie on one side of the double bond i.e. on left side the directly attached carbon is having priority over H (C>H) and

Table 1 Spectral and physical data of compounds (Step-1)

C. No.	Name	M.P. (˚C)	IR

1.1	***(Z)-4-benzylidene-2-phenyloxazol-5(4H)-one***	167-169	3078 cm^{-1} (Ar C-H *str*), 3090 (C=C-H *str*), 1790 cm^{-1} (C=O *str*), 1652 cm^{-1}(C=N *str*, oxazole), 1630, 1591 cm^{-1} (conjugated olefins).
1.2	***(Z)-4-(4-fluorobenzylidene)-2-phenyloxazol-5(4H)-one***	179-182	3073 cm^{-1} (Ar C-H *str*), 3015 cm^{-1} (C=C-H *str*), 1795 cm^{-1} (C=O *str*), 1652 cm^{-1} (C=N *str*, oxazole), 1628, 1594 cm^{-1} (conjugated olefins), 1235 cm^{-1} (C-F *str*).
1.3	***(Z)-4-(4-chlorobenzylidene)-2-phenyloxazol-5(4H)-one***	187-188	3088 cm^{-1} (Ar C-H *str*), 3015 cm^{-1} (C=C-H *str*), 1798 cm^{-1} (C=O *str*), 1655 cm^{-1} (C=N *str*, oxazole), 1632, 1597 cm^{-1} (conjugated olefins), 1090 cm^{-1} (C-Cl *str*).
1.4	***(Z)-4-(2-nitrobenzylidene)-2-phenyloxazol-5(4H)-one***	135-140	3085 cm^{-1} (Ar C-H *str*), 3020 (C=C-H *str*), 1790 cm^{-1} (C=O *str*), 1638 cm^{-1}, 1594 cm^{-1} (conjugated olefins), 1655 (C=N *str*, oxazole), 1550, 1335 cm^{-1} (N=O *str*, $ArNO_2$), 850 cm^{-1} (C-N *str*, $ArNO_2$).
1.5	***(Z)-4-(3-nitrobenzylidene)-2-phenyloxazol-5(4H)-one***	163-165	3045 cm^{-1} (Ar C-H *str*), 3016 cm^{-1} (C=C-H *str*), 1625, 1600 cm^{-1} (conjugated olefins), 1792 cm^{-1} (C=O *str*), 1650 cm^{-1} (C=N *str*, oxazole), 1520, 1345 cm^{-1} (N=O *str*, $ArNO_2$), 855 cm^{-1} (C-N *str*, $ArNO_2$).
1.6	***(Z)-4-(4-hydroxybenzylidene)-2-phenyloxazol-5(4H)-one***	170-172	3215 cm^{-1} (*br*, O-H *str*, Ar-OH), 3045 cm^{-1} (Ar C-H *str*), 3020 cm^{-1} (C=C-H *str*), 1792 cm^{-1} (C=O *str*), 1650 cm^{-1} (C=N *str*, oxazole), 1630, 1596 cm^{-1} (conjugated olefins).
1.7	***(Z)-4-(4-methoxybenzylidene)-2-phenyloxazol-5(4H)-one***	158-160	3062 cm^{-1} (Ar C-H *str*), 3010 cm^{-1} (C=C-H *str*), 2950, 2830 cm^{-1} (C-H *str*, $-OCH_3$), 1790 cm^{-1} (C=O *str*), 1652 cm^{-1} (C=N *str*, oxazole), 1632, 1600 cm^{-1} (conjugated olefins), 1245, 1030 cm^{-1} (Ar-O-CH_3 asym and sym str).
1.8	***(Z)-4-(4-methylbenzylidene)-2-phenyloxazol-5(4H)-one***	138-140	3068 cm^{-1} (Ar C-H *str*), 3000 cm^{-1} (C=C-H *str*), 2910, 2860 cm^{-1} (C-H *str*, CH_3), 1785 cm^{-1} (C=O *str*), 1650 cm^{-1}(C=N *str*, oxazole), 1630, 1600 cm^{-1} (conjugated olefins).
1.9	***(Z)-4-(4-(dimethylamino)benzylidene)-2-phenyloxazol-5(4H)-one***	158-160	3070 cm^{-1} (Ar C-H *str*), 3012 cm^{-1} (C=C-H *str*), 1782 cm^{-1} (C=O *str*), 1655 cm^{-1} (C=N *str*, oxazole), 1628, 1598 cm^{-1} (conjugated olefins), 1325 cm^{-1} (C-N str, Ar-N$(CH_3)_2$.
1.10	***(Z)-4-(furan-2-ylmethylene)-2-phenyloxazol-5(4H)-one***	158-162	3057 cm^{-1} (Ar C-H *str*), 3010-3000 cm^{-1} (multiple bands for Furan), 3015 cm^{-1} (C=C-H *str*), 1640, 1594 cm^{-1} (conjugated olefins), 1789 cm^{-1} (C=O *str*), 1655 cm^{-1}(C=N *str*, oxazole).

on the right side double-bonded nitrogen having priority over carbon (N>C), according to the Cahn-Ingold-Prelog convention for a given stereocenter.



In the IR spectra of synthesized compounds **2.1-2.10** apart from the peaks obtained for aromatic and olefinic functional groups, as seen above in step-1, two peaks which confirmed the formation of imidazole ring are peaks obtained for secondary amine and ketone with absence of peaks for lactone ring. Heteroaromatics containing N-H group absorb in the region of 3500-3220 cm^{-1} generating a band of weak intensity. Absorption in this region depends on degree of hydrogen bonding and hence upon the physical state of the sample or polarity of the solvent.

In the proton NMR spectra different types of protons can be accounted *viz.* aromatic, olefinic and amine proton. The chemical shift value for the single proton of the olefinic group should appear as a singlet at δ 7.15; the chemical shift value is calculated using base value as 5.28, which is added to the values of functional groups at cis, trans and germinal positions to the olefinic hydrogen. The values do not differ much as compared to the chemical shift values obtained from the spectral data, for the synthesized compounds. The small difference is attributed to conjugation of double bond with aromatic ring and the heterocyclic ring. The singlet was obtained as there are no neighboring protons to couple with the olefinic hydrogen. A broad and weak singlet is also obtained for the proton attached to heterocyclic nitrogen which is attributed to the proton-exchange rate on nitrogen atom. There are two aromatic rings possessing constant chemical shift values, one depending on substitution and the other is un-substituted. Compound 2.1 is only mono substituted; compound 2.4 and 2.5 are ortho-para and meta-para disubstituted while others are substituted at the para positions. The values are obtained taking shielding and deshielding effect of the neighboring groups into consideration. Physical data and spectral values are discussed in Table 2 and 3.

Table 2 Spectral and physical data of compounds (Step-2)

C. No.	Name	Molecular Formula	Yield	M. P.	R_f
2.1	***(Z)-4-benzylidene-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{12}N_2O$	98 %	160 - 164 ˚C	0.48
2.2	***(Z)-4-(4-fluorobenzylidene)-2-phenyl-1H-***	$C_{16}H_{11}FN_2O$	92 %	80-84˚C	0.7

	imidazol-5(4H)-one				
2.3	***(Z)-4-(4-chlorobenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{11}ClN_2O$	94 %	152 - 154 ˚C	0.33
2.4	***(Z)-4-(2-nitrobenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{11}N_3O_3$	90 %	205 - 208 ˚C	0.7
2.5	***(Z)-4-(3-nitrobenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{11}N_3O_3$	90 %	152 - 155 ˚C	0.56
2.6	***(Z)-4-(4-hydroxybenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{12}N_2O_2$	98.3%	218 - 222 ˚C	0.36
2.7	***(Z)-4-(4-methoxybenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{16}H_{12}N_2O_2$	92.3%	167 - 170 ˚C	0.45
2.8	***(Z)-4-(4-methylbenzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{17}H_{14}N_2O$	98 %	190 - 193 ˚C	0.66
2.9	***(Z)-4-(4-(dimethylamino)benzylidene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{18}H_{17}N_3O$	99.3%	175 - 180 ˚C	0.65
2.10	***(Z)-4-(furan-2-ylmethylene)-2-phenyl-1H-imidazol-5(4H)-one***	$C_{14}H_{10}N_2O_2$	99.3%	178 - 180 ˚C	0.6

Fig 1 Ligand-receptor interaction diagram for compound 2.2

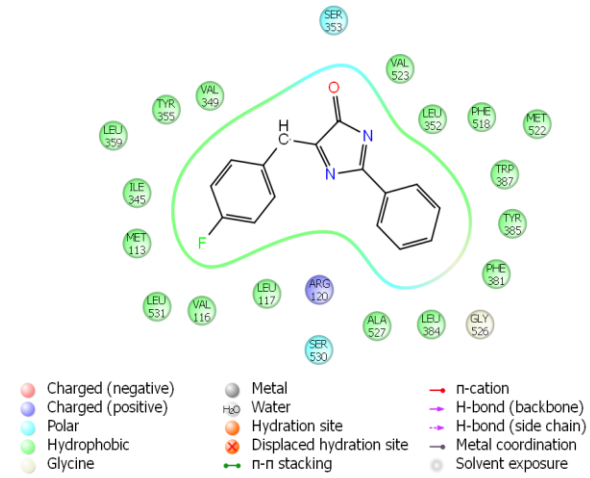


Fig 2 Hydrophobic enclosure of ligand (2.2) in receptor cavity

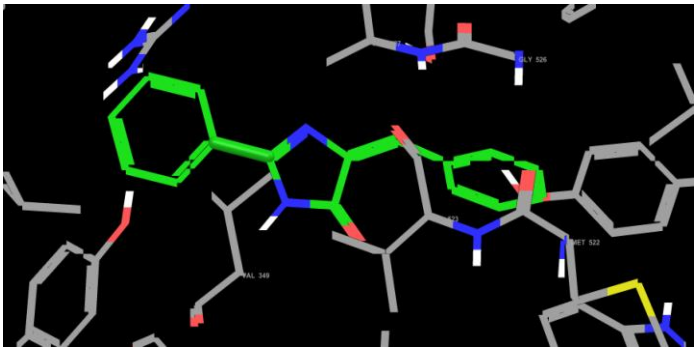


Fig 3 Rotatory penalty for bond joining aromatic ring and imidazole ring for ligand 2.2

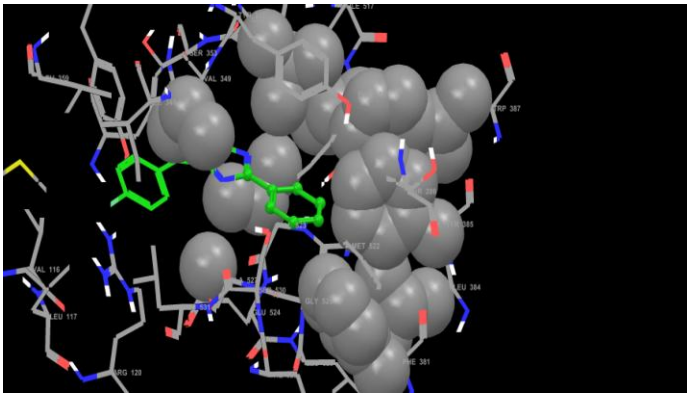


Table3 Spectral data of synthesized compounds (Step-2)

C. No.	IR	NMR	Mass
2.1	3218 cm^{-1} (>NH, imidazole), 1652 cm^{-1} (>C=O, imidazole)	δ 7.2 (s, 1H, ArC=C*H*-), δ 7.29-7.46 (m, 5H, Ar*H*), δ 7.51-7.67 (m, 5H, Ar*H*), δ 9.83 (s, 1H, -N*H*).	M^+ 248.09 (100.0%), 249.10 (17.5%), 250.10 (1.8%)
2.2	3230 cm^{-1} (>NH, imidazole), 1655 cm^{-1} (>C=O, imidazole)	δ 6.98 (s, 1H, ArC=C*H*-), δ 6.9-7.28 (m, 4H, Ar*H*), δ 7.31-7.66 (m, 5H, Ar*H*), δ 10.06 (s, 1H, -N*H*).	M^+ 266.09 (100.0%), 267.09 (17.5%), 268.09 (1.7%)
2.3	3210 cm^{-1} (>NH, imidazole), 1662 cm^{-1} (>C=O, imidazole)	δ 7.1 (s, 1*H*, ArC=C*H*-), δ 7.34-7.6 (m, 4*H*, Ar*H*), δ 7.51-7.66 (m, 5*H*, Ar*H*), δ 10.0 (s, 1H, -N*H*).	---
2.4	3225 cm^{-1} (>NH, imidazole), 1657 cm^{-1} (>C=O, imidazole)	δ 7.22 (s, 1*H*, ArC=C*H*-), δ 7.52-8.14 (m, 4*H*, Ar*H*), δ 7.51-7.66 (m, 5*H*, Ar*H*), δ 9.02 (s, 1H, -N*H*).	M^+ 293.08 (100.0%), 294.08 (18.5%)
2.5	3225 cm^{-1} (>NH, imidazole), 1657 cm^{-1} (>C=O, imidazole)	δ 7.05 (s, 1*H*, ArC=C*H*-), δ 7.69-8.34 (m, 4*H*, Ar*H*), δ 7.51-7.66 (m, 5*H*, Ar*H*), δ 9.4 (s, 1H, -N*H*).	---
2.6	3200 cm^{-1} (>NH, imidazole), 1650 cm^{-1} (>C=O, imidazole), 3235 cm^{-1} (*br*, O-H str, Ar-O*H*)	δ 7.12 (s, 1*H*, ArC=C*H*-), δ 6.82-7.32 (m, 4H, Ar*H*), δ 7.53-7.68 (m, 5H, Ar*H*), δ 9.8 (s, 1H, -N*H*), δ 12.9 (br, 1H, Ar-O*H*).	---
2.7	3320 cm^{-1} (>NH, imidazole), 1658 cm^{-1} (>C=O, imidazole)	δ 3.90 (s, 3H, Ar-OCH_3), δ 7.05 (s, 1*H*, ArC=C*H*-), δ 6.7-7.19 (m, 4*H*, Ar*H*), δ 7.51-7.68 (m, 5H, Ar*H*), δ 9.82 (s, 1H, -N*H*).	M^+ 264.09 (100.0%)
2.8	3208 cm^{-1} (>NH, imidazole), 1660 cm^{-1} (>C=O, imidazole)	δ 2.42 (s, 3H, Ar-CH_3), δ 7.1 (s, 1*H*, ArC=CH-), δ 7.22-7.41 (m, 4*H*, ArH), δ 7.55-7.61 (m, 5*H*, ArH), δ 9.79 (s, 1*H*, -NH).	---
2.9	3228 cm^{-1} (>NH, imidazole), 1658 cm^{-1} (>C=O, imidazole)	δ 3.12 (s, 6H, ArN-(CH_3)$_2$, δ 6.92 (s, 1*H*, ArC=CH-), δ 6.87-7.28 (m, 4*H*, ArH), δ 7.55-7.68 (m, 5*H*, ArH), δ 9.79 (s, 1*H*, -NH).	M^+ 291.14 (100.0%)
2.10	3230 cm^{-1} (>NH, imidazole), 1651 cm^{-1} (>C=O, imidazole)	δ 6.66-7.8 (m, 3*H*, 2-furyl), 6.69 (s, 1*H*, ArC=CH-), δ 7.57-7.68 (m, 5*H*, ArH), δ 9.7 (s, 1*H*, -N*H*).	M^+ 238.07 (100.0%)

In silico molecular docking studies revealed that compound 2.1, 2.2, 2.3, 2.8 and 2.10 obtain good Glide scores (Table 4). Compound **2.2,** having highest G score of 8.7 was awarded for enclosure of its aromatic group by resides of tyrosine (355, 385), leucine (352, 384), isoleucine (345), tryptophan (387) phenylalanine (381, 518), valine (523, 349) and alanine (527) as shown in Figure 1. Hydrophobic atoms on the protein that are necessary for recognition of hydrophobic enclosure are displayed in CPK representation in gray and hydrophobic atoms on the ligand necessary for hydrophobic enclosure are displayed in green in ball and stick representation (Figure 2). The enclosure surrounds the non polar region of aromatic ring which contributes

towards binding affinity of the molecule and hence increases the glide score. The major contribution to the energy minima (-1.5) comes from the sitemap-ligand complementary terms exhibiting comfortability of the ligand – receptor interaction. The molecule was penalized for having free rotation around a single bond (Figure 3). *In silico* toxicity study (Table 5) revealed that compound 2.4, 2.5 and 2.6 may possess high toxicity in terms of oncogenicity and mutagenicity.

Table 4 Docking scores of all the synthesized compounds

ligand	G score[a]	Lipophilic EvdW[b]	PhobEn[c]	HBond[d]	Electro[e]	Sitemap[f]	LowMW[g]	Penalties[h]	RotPenal[i]	Similarity[j]
2.1	-8.3	-4.56	-2.7	0	-0.04	-0.62	-0.5	0	0.12	0.1
2.2	-8.72	-4.4	-2.65	0	0.01	-1.5	-0.5	0	0.33	0.09
2.3	-8.51	-5.38	-2.2	0	0.06	-0.6	-0.5	0	0.1	1
2.4	-7.33	-4.67	-1.41	0	-0.25	-0.68	-0.5	0	0.18	1
2.5	-5.3	-3.8	-1.99	0	-0.02	-0.67	-0.5	1.5	0.18	0.26
2.6	-7.63	-4.22	-2.5	0	0.01	-0.64	-0.5	0	0.22	0.92
2.7	-7.53	-4.18	-2.04	0	0.04	-1.15	-0.5	0	0.3	0.57
2.8	-8.5	-5.54	-2.17	0	0.09	-0.6	-0.5	0	0.22	1
2.9	-6.73	-5.19	-1.56	0	-0.06	-0.61	-0.5	1	0.18	1
2.10	-8.11	-4.46	-2.27	-0.16	-0.06	-1.06	-0.5	0	0.39	0.11

[a]Glide Score; [b]LipophilicEvdW- Lipophilic term derived from hydrophobic grid potential and fraction of the total protein-ligand vdW energy; [c]PhobEn- Hydrophobic enclosure reward; [d]HBond- Chem core H bond term; [e]Electro- electrostatic reward; [f]Sitemap- ligand complementarity terms; [g]LowMW- reward for ligand with low molecular weight; Penalties[h]- Penalty for polar atom burial; RotPenal[i]- Penalty for roation about C-C bond; Similarity[j]- Similarity algorithms provide a mechanism for quantifying how alike or unlike two molecules are.

Table 5 Toxicity studies predicted using PALLAS software

C. No.	Toxicity	Max. toxicity	Oncogenicity	Mutagenicity	Teratogenicity	Membrane-irritation	Sensitization	Immunotoxicity	Neurotoxicity
2.1	NP	34	0	0	34	0	0	0	0
2.2	NP	34	0	0	34	0	0	0	0
2.3	NP	34	0	0	34	0	0	0	0
2.4	NP	67	64	67	34	0	29	0	0
2.5	NP	67	64	67	34	0	29	0	0
2.6	NP	53	0	29	34	53	0	0	29
2.7	NP	34	0	0	34	0	0	0	0
2.8	NP	34	0	0	34	0	0	0	0
2.9	NP	34	0	0	34	0	0	0	0
2.10	NP	34	0	0	34	0	0	0	0

*NP- Not Probabale

CONCLUSION

Ten compounds were synthesized efficiently using microwave as an alternate source of energy. It was found that quite a few compounds were effective in terms of Glide score. Further anti-inflammatory and analgesicl studies of these compounds will be carried out to determine the same. If the same were found effective more of these compounds will be synthesized using microwave as it saves time and leads to less wastage of chemicals.

References

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