DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL CHALCONE DERIVATIVES AS ANTI-INFLAMMATORY AGENTS

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Chalcones are natural or synthetic 1,3-diaryl-2-propen-1-ones belonging to the flavonoid family of natural products. Chemically, they contain an open-chain flavonoid skeleton in which two aromatic rings are linked by a three-carbon α, β-unsaturated carbonyl system. They have been reported to possess many useful properties including anti-inflammatory, antimicrobial, antioxidant, antiviral and anticancer activities, therefore representing a class with enormous therapeutic potential. The classic non-steroidal anti-inflammatory drugs (NSAIDs) which are non-selective in their inhibition of cyclooxygenase (COX) isoforms as well as the newer NSAIDs that are selective COX-2 inhibitors have been well documented to cause severe side-effects. Utilizing the chalcone framework in an effort to develop novel anti-inflammatory agents, we are attempting to systematically establish structure activity relationships (SAR) of the scaffold. Accordingly, a chalcone library was designed based on physico-chemical properties like polarity, sterics and electronics. The cyclooxygenase targets and ligands were minimized using CHIRON Energy Minimization Server and CORINA software respectively. Energy-minimized conformations were docked using Arguslab and Autodock. Those showing the best docking score and following Lipinski rule of five were selected as lead molecules for synthesis that was achieved via a Claisen-Schmidt condensation procedure. These are being evaluated as possible anti-inflammatory agents targeting COX-1 and COX-2.
SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF A CYCLIC HEXAPEPTIDE

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A natural glycine-rich cyclic hexapeptide - dichotomin D, previously isolated from the roots of Stellaria dichotoma, was synthesized by coupling of tripeptide units Boc-Gly-L-Phe-L-Tyr-OH and L-Ile-Gly-L-Val-OME followed by cyclization of linear hexapeptide segment. Required tripeptide units were prepared by coupling of Boc-protected dipeptides viz. Boc-Gly-L-Phe-OH and Boc-L-Ile-Gly-OH with respective amino acid methyl ester hydrochlorides L-Tyr-OMe.HCl and L-Val-OMe.HCl. Cyclization of linear hexapeptide unit was done by pentafluorophenyl ester method. The structure of synthesized cyclooligopeptide was elucidated by spectral analysis including FTIR, 1H/13C NMR, ESIMS/MS as well as elemental analysis. The newly synthesized cyclopeptide was screened for its anthelmintic and antifungal potential. Synthesis of cyclohexapeptide was accomplished with good yield utilizing diisopropylcarbodiimide (DIPC) as coupling agent. Newly synthesized peptide was found to exhibit potent anthelmintic activity against earthworms M. konkanensis and Eudrilus sp. Good activity against dermatophytes M. audouinii and T. mentagrophytes and moderate bioactivity against pathogenic C. albicans was also observed for newly synthesized cyclooligopeptide. Solution phase technique employing DIPC and triethylamine (TEA) as base proved to be effective for the synthesis of natural cyclohexapeptide.
SYNTHESIS AND EVALUATION OF NOVEL BRAIN TARGETING CHEMICAL DELIVERY SYSTEMS OF NORFLOXACIN

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The present investigation involves synthesis of novel chemical delivery systems/derivatives of selected fluoroquinolone antibacterial drug - norfloxacin. All the newly synthesized compounds were characterized by suitable spectroscopic methods such as IR, NMR, MS, CHN analysis etc. The data obtained was in full agreement with the proposed structures. The synthesized compounds were evaluated for their partition coefficients and log P values were determined which were significantly higher than the parent drugs. Compounds were investigated for their chemical oxidation studies by adopting hydrogen peroxide mediated method and silver nitrate mediated oxidation method. All the synthesized chemical delivery systems of norfloxacin demonstrated high oxidative conversion rates by hydrogen peroxide and silver nitrate mediated chemical methods. This indicated that the chemical delivery systems have been appropriately developed. The selected compounds exhibited significantly higher concentration of free drugs in rat brains when compared to their parent drugs.
**N-phthalyl ethyl acetate: As a product and as a precursor for the synthesis of phthalimide derivatives**

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A novel approach was designed for synthesis of an imide compound containing two carbonyl groups bound to 1’ amine, namely phthalimide, which was used as a starting material for the synthesis of its ester derivative, N-phthalyl ethyl acetate. This N-phthalyl ethyl acetate was further used for the synthesis of series of its derivatives i.e. 2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl) acetyl] hydrazine carbothioamide (BPM1) and 2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-N-phenylacetamide (BPM2) by using thiosemicarbazide and aniline respectively. These designed compounds were synthesized with satisfactory percentage yields and chemical structures were characterized and confirmed by using chromatography i.e. TLC, spectroscopy i.e. IR, NMR and elemental analysis.
Quinazoline derivatives occupy a distinct and unique place in the medicinal chemistry as they possess diverse biological activities. As on date, about 25 clinically used drugs are quinazoline derivatives. This review has presented a comprehensive detail of quinazoline derivatives which are under clinical trial. Appreciable number of heterocyclic compounds containing nitrogen atom obtained by laboratory synthesis have turned out to be potential chemotherapeutic and pharmacotherapeutic agents. Various useful synthetic analogs with improved therapeutic properties can be obtained from a single lead compound by structural modification. The same principle is applicable to quinazolines. Quinazoline nucleus has attracted the attention of medicinal chemists due to its diverse biological activities. The biological activities of quinazoline derivatives have been reviewed. There are many quinazoline derivatives which are under different phases of trial i.e. pre-clinical trial, phase I trial, phase II trial, phase III trial. In this review, present authors emphasize on quinazoline derivative which are currently under Phase I trial, Phase II trial and Phase III trial and are being investigated for further development.
Computer assisted drug design (CADD): applications over physical model

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Computer assisted drug design (CADD) has two fundamental roles to play in drug research; one is lead discovery and another is lead development. Manipulation of computer models is much superior to the use of traditional physical models as mathematical models using quantum mechanics or force field methods better account for the inherent flexibility of molecules than do hard sphere physical models. It is easy to superimpose one or more molecular models on a computer and to color each structure separately for ease of viewing. Medicinal chemists use the superimposed structures to identify the necessary structural features and the 3D orientation (pharmacophore) responsible for the observed biological activity. The display of the multiple conformations available to a single molecule can provide valuable information about the conformational space available to drug-like molecules. Rather than measuring bond distances with ruler, computer generated molecular display is easy. Once a molecular structure has been entered into a molecular modeling software program, the structure can be viewed from any desired perspective. The dihedral angles can be rotated to generated new conformations and functional groups can be eliminated or modified almost effortlessly. Molecular features (bond lengths, bond angles, non-bonded distances etc) can be calculated readily from the stored 3D coordinates.
SYNTHESIS OF PYRAZINE CARBOXAMIDE DERIVATIVES AND THEIR BIOLOGICAL EVALUATION

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The pyrazine ring is a part of many polycyclic compounds of biological or industrial significance. Pyrazines have long been of interest to medicinal chemists. Their derivatives, many of which are natural products; have proven to be useful as antibiotics, antioxidants, diuretics and anti-tumor agents. The minimal structure of pyrazine ring with an acyl moiety is sufficient for fatty acid synthase type I (FAS I) and antimycobacterial activity of some pyrazine carboxylic acid derivatives. In the present study, synthesis of binuclear analogues with the -CONH- bridge was carried out. The amide function is based on the bivalent moiety -CONH-, which can form centrosymmetric dimer pairs with the peptidic carboxamido group of some peptides, needed for binding to the receptor site, possibly by forming a hydrogen bond. The pyrazinamide derivatives have been synthesized and evaluated for the antimycobacterial and antifungal activity. All the eight derivatives were synthesized by condensation of the corresponding chlorides of pyrazine-2-carboxylic acid with various ring-substituted aminopyridines. Primary screening of all compounds were conducted at 6.25 µg/ml against Mycobacterium tuberculosis strain H37Rv. For antifungal evaluation, all the compounds showed the activity at 50 µg/ml. Pyrazine-2-carboxylic acid (5-chloro pyridine-2-yl) amide and pyrazine-2-carboxylic acid (5-nitro pyridine-2-yl) amide have shown both the antimycobacterial and antifungal activity.
A FACILE ONE-POT SYNTHESIS OF NOVEL ISOINDOLE DERIVATIVES OF BIOLOGICAL INTEREST

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A novel and efficient strategy for the systematic synthesis of a series of derivatives of N-phthalyl ethyl acetate namely [(1,3-dioxo-1,3-dihydro-2H-isoindole-2-yl)-N-phenylacetohydrazide (BPM3)], [N’-(2,4-dinitrophenyl)-2-(1,3-dioxo-1,3-dihydro-2H-isoindole-2-yl)acetohydrazide (BPM4)], [2-(1,3-dioxo-1,3-dihydro-2H-isoindole-2-yl)-N-(phenyl carbomoyl) acetamide (BPM5)], and [2-(1,3-dioxo-1,3-dihydro-2H-isoindole-2-yl)-N-(4-nitrophenyl)acetamide (BPM6)] is reported with minimal number of steps. Simple and readily synthesized compound used as a starting material N-phthalyl acetate with phenyl hydrazine, 2,4-dinitrophenyl hydrazine, phenyl urea, 4-nitroaniline (1° amine containing compound) respectively. These designed compounds were synthesized with satisfactory percentage yields. Different functional group tests like test for nitrogen were performed for the characterization of the functional groups present in the structure of compound. Melting point determination of all synthesized derivatives was done to find out their melting range. Other than functional group test and melting point determination, qualitative analysis for the structural stability and characterization of purity of these synthesized compounds was also performed by using analytical techniques like chromatography (TLC) and different spectral techniques like infra red and nuclear magnetic resonance.
SYNTHESIS AND BIOLOGICAL EVALUATION OF COUMARIN DERIVATIVES

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In the present study, different coumarin derivatives were prepared by treating 3-acetylcoumarin with various 4-arylthiosemicarbazide in ethanol and few drops of glacial acetic acid media, which yields N-aryl (3-acetylcoumarin)thiosemicarbazones. The products have been purified by recrystallization with suitable solvent. The compounds have been characterized on the basis of their analytical and spectral properties. All synthesized compounds were characterized by TLC, IR and mass spectral properties. The synthesized compounds were screened for anti-bacterial, anti-fungal and anti-diabetic activity. Tested compounds exhibited moderate to good anti-bacterial activity against both gram-positive and gram-negative bacteria. Few of the new compounds exhibited anti-fungal activity equal to standard drug against Aspergillus flavus and Candida albicans. Selected new compounds exhibited moderate to significant anti-diabetic activity when compared with control. A single intraperitoneal administration of alloxan at dose of 120 mg/kg produced diabetes in rats, which was evident by observing marked elevation in blood glucose level (hyperglycemia) in diabetic control group, when compare to normal control group.
PHARMACOPHORE MODELING AND 3D-QSAR STUDIES ON (E)-ALPHA-BENZYLTHIO-CHALCONES AS INHIBITOR OF BCR-ABL KINASE

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Three dimensional pharmacophore modeling studies were performed on a diverse set of 34 molecules of (E)-α-benzylthio-chalcone derivatives that demonstrate anticancer activity by blocking BCR-ABL phosphorylation in leukaemic cells. The three-dimensional QSAR (3D-QSAR) study based on the principle of the alignment of pharmacophoric features by PHASE module of Schrodinger suite has been carried out on the same set of molecules. Four point pharmacophore with one hydrogen bond acceptor, one hydrophobic group and two aromatic rings as pharmacophoric features. Amongst them the pharmacophore hypothesis HRR9 yielded a statistically significant 3D-QSAR model with 0.89 as $R^2$ value and was considered to be best pharmacophore hypothesis. The developed pharmacophore model was externally validated by predicting the activity of test set molecules. The squared predictive correlation coefficient of 0.74 was observed between experimental and predicted activity values of test set molecules. The geometry and features of pharmacophore were expected to be useful for the design of selective BCR-ABL kinase inhibitors.
3D-QSAR STUDIES OF FURAN AND MORPHOLINO DERIVATIVES AS INHIBITOR OF STAPHYLOCOCCUS AUREUS SORTASE A

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Pharmacophore mapping studies were undertaken for a set of 28 furan, thiophene, and morpholino derivatives as staphylococcus aureus Sortase A inhibitors. Three point pharmacophores with one hydrogen bond acceptor, and two aromatic rings as pharmacophoric features were developed. Amongst them the pharmacophore hypothesis ARR11 yielded a statistically significant 3D-QSAR model with 0.8431 as $R^2$ value and was considered to be the best pharmacophore hypothesis. The developed pharmacophore model was externally validated by predicting the activity of test set molecules. The squared predictive correlation coefficient of 0.16 was observed between experimental and predicted activity values of test set molecules. The geometry and features of pharmacophore were expected to be useful for the design of selective $S. aureus$ Sortase A inhibitors.

POSTER PRESENTATION
THREE DIMENSIONAL PHARMACOPHORE MAPPING OF PYRAZOLE DERIVATIVES AS ANTIPROLIFERATIVE AGENTS

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A set of 36 pyrazoles were taken and pharmacophore mapping studies was carried out on them as antiproliferative agents in human ovarian adenocarcinoma A2780 cells, human lung carcinoma A549 cells, and murine P388 leukemia cells. Six point Pharmacophore model with one hydrogen bond acceptor, two hydrogen bond donor as pharmacophoric features were developed. The pharmacophore hypothesis AHH.14 yielded a statistically significant 3D-QSAR model with 0.9093 as $R^2$ value and was considered to be the best pharmacophore hypothesis. External validation of the developed pharmacophore model's test set molecules was carried out by predicting their activity. The squared predictive correlation coefficient of 0.63 was observed between experimental and predicted activity values of test set molecules. The geometry and features of pharmacophore were expected to be useful for the design of selective antiproliferative agents.
SYNTHESIS OF DIHYDROPYRIMIDINONES AS NOVEL ANTI-BACTERIAL AND ANTHELMINTIC AGENTS

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Dihydropyrimidin-2(1H)-one (DHPM) belongs to one of the important class of therapeutic and pharmacological active compound. A novel series of dihydropyrimidin-2(1H)-one compounds were synthesized through the multicomponent reactions of aldehydes, ethyl acetoacetate and urea, followed by the heterogeneous catalyzed reaction of the intermediate with phthalimide, benzimidazole, imidazole in DMF. All the compounds synthesized were characterized by using IR and NMR spectral data. All the newly synthesized compounds were evaluated for in vitro antibacterial and anthelmintic activities. In vitro studies show that most of the compounds exhibit the moderate activity. Compounds ethyl 1,3-bis((1H-benzo[d]imidazol-1-yl)methyl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-carboxylate and ethyl 1,3-bis((1H-benzo[d]imidazol-1-yl)methyl)-4-(4-(dimethylamino)phenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-carboxylate with 26 mm zone of inhibition exhibit maximum antibacterial activity against Staphylococcus aureus. Compound ethyl 1,3-bis((1,3dioxoindolin-2-yl)methyl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate with 24 mm zone of inhibition exhibit activity against Escherichia coli. Compound ethyl 1,3-bis((1,3dioxoindolin-2-yl)methyl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate had the comparable anthelmintic activity with the standard drug (Piperazine citrate). Compound ethyl 1,3-bis((1,3dioxoindolin-2-yl)methyl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate had 44±0.54 min as mean paralyzing time and 58±0.59 min as death time whereas the standard drug had 40±0.77 min as mean paralyzing time and 62±0.67 min as death time.

POSTER PRESENTATION
Biological Activities of Hydantoin Derivatives in New Millennium

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Hydantoin which is also known as glycolylurea is a heterocyclic organic compound that can be thought of as a cyclic "double-condensation reaction" product of glycolic acid and urea. Hydantoins are chiefly used in the treatment of seizures associated with epilepsy: a neurological dysfunction in which excessive surges of electrical energy are emitted in the brain. While hydantoins control the seizures associated with epilepsy, there is no known cure for the disorder. For the treatment of seizures, hydantoins may be used alone or in combination with other anti-epileptic drugs (AEDs) or anticonvulsants. Phenytoin, mephenytoin, ethotoin and fosphenytoin are the individual hydantoin anticonvulsants which are marketed under several brand names, including cerebyx, dilantin, mesantoin, peganone and phentek. However, hydantoins are not only anticonvulsant but are present in many of the bioactive heterocyclic compounds that are of wide interest because of their diverse biological and clinical applications. The researchers have synthesized a variety of hydantoin derivatives and screened them for various biological activities viz. anticonvulsant, anticancer, anti-HIV, immunomodulatory, antimycobacterial, antimicrobial, antihypertensive, antiarrhythmic, as well as antidepressant activities.
NEW THIAZOLIDIN-4-ONE ANALOGUES CONTAINING PYRIDINE RING: SYNTHESIS, BIOLOGICAL EVALUATION AND QSAR STUDIES

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A series of pyridine derivatives of thiazolidin-4-ones (4a-4o) have been synthesized and characterized on the basis of elemental and spectral analysis. Synthesized compounds were evaluated for anti-inflammation and analgesic activity. The results showed that compound 2-[4-methylphenylimino]-5-(1H-pyridin-2-ylmethylidene)-1,3-thiazolidin-4-one (4d), 2-(2,4-dinitrophenylhydrazinylidine)-5-(1H-pyridin-2-yl-methylidene)-1,3-thiazolidin-4-one (4h) and 2-[3-nitrophenylimino]-5-(1H-pyridin-2-yl-methylidene)-1,3-thiazolidin-4-one (4j) exhibited good anti-inflammatory activity and analgesic activity. Compound 4h was found to be most active compound of the series with an interesting dual anti-inflammatory and analgesic activity. Docking simulation was performed to position synthesized compounds into the active site of COX-2. The relationships of energy-based docking score with analgesic and anti-inflammatory activities were also investigated using linear regression method. The QSAR models with R² of 0.621 and 0.740 were developed for analgesic and anti-inflammatory activities respectively.

POSTER PRESENTATION
SYNTHESIS, ANTIBACTERIAL AND ANTHELMINTIC EVALUATION OF NOVEL 2,4-THIAZOLIDINEDIONES

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In the present study, a series of novel N-substituted thiazolidine-2,4-diones were synthesized and evaluated for their antibacterial and anthelmintic activities. 5-indol-3-methylidene-2,4-thiazoizolidindione was synthesized by taking 2,4-thiazolidinedione and indole-3-carboxaldehyde in acetic acid and sodium acetate were added. After this, the reaction mixture was refluxed for 12 hrs. Sodium salt of 5-indol-3-methylidene-2,4-thiazoizolidinone was prepared in the next step. Finally, the target compounds were synthesized by refluxing sodium salt of 2,4-thiazolidinedione and N-chloroacetamide derivatives in DMF-EtOH. The structures of the target compounds were confirmed by IR and NMR spectral data. Antibacterial evaluation was determined by measuring the zone of inhibition. All the synthesized compounds exhibited the moderate antibacterial activities. Compound 5-indol-3-methylidene-2,4-thiazoizolidinone-acetamide with 22 mm zone of inhibition was the most potent derivative against the Bacillus subtilis. Compound N-[2-(2-florophenyl)-2-[(5Z)-5-(1H-indole-3-ylmethylidene)-2,4-dioxo-1,3-thiazolidin-3-yl]-acetamide (16 mm) and 2-[5z-5-(1H-indol-3-ylmethylidene)-2,4-dioxo-1,3-thiazolidin-3-yl]-N-(4-methoxyphenyl)-acetamide (15 mm) had a significant zone of inhibition against Pseudomonas aeruginosa. The evaluation of anthelmintic activity was carried out by Garg’s method against Eisenia fetida. Compound N-(2-florophenyl)-2-[(5Z)-5-(1H-indole-3-ylmethylidene)-2,4-dioxo-1,3-thiazolidin-3-yl]-acetamide had comparable anthelmintic activity with the standard drug. This compound had 54±0.4 min as mean paralyzing time and 78±0.73 min as death time.
SYNTHESIS OF NOVEL BENZOTHIAZOLE SUBSTITUTED DRUG DERIVATIVES AND THEIR ANTHelmINTIC EVALUATION

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A series of novel derivatives was synthesized by clubbing 6-substituted 2-amino benzothiazoles with pyrazinamide, nicotinamide and isoniazid via thioamide linkage which were found to have anthelmintic activity. Benzothiazoles used in synthesis were prepared by using substituted anilines as starting material. Synthesized compounds were evaluated for their anthelmintic activity against Eisemia foetida. The major findings indicated that all of the synthesized compounds exhibited promising anthelmintic activity but among all, 1-(6-nitro-1,3-benzothiazol-2-yl)-carbothiomethylpyridine-2-carbothioamide was found to be most potent anthelmintic agent with a mean paralyzing time of 27.00±2.70 and a mean death time of 43.80±1.39 when compared with the standard piperazine citrate, with a mean paralyzing time of 24.40±1.03 and a mean death time of 34.80±1.02 at a concentration of 200 mg/100 ml.
SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SOME NOVEL SUBSTITUTED IMIDAZOLE BEARING TRIAZOLE DERIVATIVES

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Imidazole and triazole nuclei are well known heterocycles which are integral part of a variety of medicinal agents exhibiting bioactivities. Substituted imidazole bearing triazole compounds in the literature have been found to exhibit superior pharmacological activities as compared to compounds having individual imidazole or triazole nucleus. These findings have encouraged us for synthesis of substituted imidazole bearing triazole compounds. The titled compounds (2,4,5-trisubstituted-1H-imidazole bearing triazole derivatives) were synthesized from the starting materials benzil, aromatic aldehydes, ammonium acetate and sulphanilic acid catalyst in the presence of ethanol which resulted in the synthesis of 2,4,5-trisubstituted-1H-imidazoles. These were converted into substituted imidazolyl ester derivatives. Substituted imidazolyl ester derivatives were further converted into substituted imidazolyl hydrazide derivatives which were combined with different aryl and alkyl isothiocyanates to synthesize 2,4,5-triphenyl-imidazol-1-yl-ethanoyl-substituted-aryl/alkylthiosemicarbazides which were finally converted into substituted imidazole bearing triazole derivatives. These compounds were characterized by elemental analysis, IR, 1H-NMR and mass spectral data. All the compounds were investigated for their antimicrobial activity against two Gram-positive stains (Staphylococcus aureus and Streptococcus pyogenes) and two Gram-negative stains (Escherichia coli and Klebsiella pneumoniae) which showed moderate to good activity when compared with standard drug vancomycin.

POSTER PRESENTATION
Cancer is a major ailment prevailing these days. Several types like breast cancer, breast adenocarcinoma, melanoma, non small cell lung cancer (NSCLC), osteosarcomas, and different types of tumors affect a large population across different countries of the world. Anthracyclines are important class of antibiotics and a member of a family of chemotherapeutic agents. They prevent the cell division by disrupting the structure of the DNA by either causing free radical damage of the ribose in the DNA or by intercalating into the base pairs in the minor grooves. Current scientific literature suggests that these agents and their derivatives may depict a potential role in treatment of cancer. In recent past, a number of anthracycline derivatives have been synthesized by different methods and their pharmacological activities like anti-tumor, anti-breast cancer, anti-proliferative, anti-osteosarcoma have been studied. Present paper is an earnest attempt to review the current medicinal aspects with specific context to anticancer activities of anthracycline derivatives.
SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF BENZOTHIAZOLE CLUBBED THIAZOLIDIN-4-ONE DERIVATIVES

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Thiazolidinone derivatives are traditionally known as a class of biologically active compounds. In recent years, a large number of innovative drugs containing the thiazolidinone moiety have been developed that exhibits diverse biological activities such as hypoglycemic, antineoplastic, analgesic, antiepileptic, antidegenerative, antidibetic, antifungal, antinflammatory, antimicrobial, antioxidant, antitubercular etc. The present work includes synthesis and antimicrobial activity of five new 6-fluoro-2-aminobenzothiazolyl-1,3-thiazolidin-4-ones derivatives. Compounds have been synthesized employing 4-fluoro aniline as a starting material which was reacted with potassium thiocyanate to yield 4-aminobenzothiazole which was reacted with chloroacetyl chloride to yield chloroacetamide. Then chloroacetamide was reacted with ammonium thiocyanate to yield thiazolidinone which was reacted with different aldehydes to yield respective derivatives. The chemical structures of all synthesized compounds were confirmed by IR and ¹H-NMR spectral data. All the synthesized compounds were tested against selected Gram positive, Gram negative and fungal species. Most of the compounds showed significant activity. Compound 5-(4-dimethylaminobenzylidene)-2-(6-fluorobenzothiazol-2ylimino)-1,3-thiazolidin-4-one was most potent derivative against Bacillus subtilis and Escherichia coli.
SYNTHESIS AND ANTIOXIDANT ACTIVITY OF NOVEL AMINOBENZOTHIAZOLYL-1,3-THIAZOLIDIN-4-ONE DERIVATIVES

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The aim of present research work was to synthesize a new series of amino benzothiazolyl-1,3-thiazolidin-4-ones capable of suppressing oxidation of oxidisable substrates (antioxidant activity). The compounds have been synthesized by treating aniline with potassium thiocynate in the presence of glacial acetic acid to yield benzothiazoles. It was further refluxed with chloroacetyl chloride in chloroform for 12 h to give acetamide. Acetamide in presence of aminothiocynate in ethanol produced 6-substituted-(1,3-benzothiazol-2-ylimino)-1,3-thiazolidin-4-ones, which was refluxed for 24-48 h in the presence of aromatic aldehyde along with piperidine give final products (5a-e). The synthesized compounds were purified by recrystallization and were characterized by melting point, IR, 1H-NMR and TLC. These compounds were tested for their antioxidant activity by evaluation method of scavenging of hydrogen peroxide and by 1,1-diphenyl-2-picryl hydrazyl (DPPH) antioxidant assay by using BHA and ascorbic acid as reference standards. Compound 5b was the most active with 61.53% scavenging of hydrogen peroxide at 100 microgram concentration of drug, followed by compound 5c which showed 47.94% scavenging at 100 microgram. The same compounds were observed to be most active agents in the DPPH antioxidant assay. In general, all the synthesized compounds exhibited moderate antioxidant activity.
SYNTHESIS AND EVALUATION OF ANALGESIC ACTIVITY OF AMINO ACID CLUBBED PRODRUGS OF NAPROXEN

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Naproxen, chemically known as (+)-6-methoxy-α-methyl-2-naphthaleneaceticacid, is a nonsteroidal anti-inflammatory drug (NSAID) having analgesic and antipyretic activity. It is frequently used for treatment of rheumatoid arthritis and osteoarthritis but also depicts some side effects on prolonged use which leads to gastro-intestinal irritation, bleeding and ulceration. To overcome these side effects a new series of prodrugs of naproxen has been synthesized by the reaction of naproxen with thionyl chloride to yield acid chloride which was further reacted with glucose to form the glucosyl naproxen. Tetra-acetate of glucosyl naproxen was synthesized and finally reacted with different amino acids to yield the various prodrugs of naproxen. These newly synthesized compounds were screened for their analgesic activity and for possible GI toxicity. Analgesic activity of these compounds was evaluated by tail immersion method using swiss albino mice. Latency period was expressed as percentage protection by standard and synthesized compounds with control group. Some of the synthesized compounds were found to have analgesic activity comparable to that of naproxen. Among all of the synthesized compounds, 3-(3,4-dihydroxyphenyl)-2-N-{6-[2”-methyl-1”-(6-methoxyphth-1-yl)]ethoxy}-2’3’4’,5’-tetraacetylhex-1’-yl-2-iminopropanoic acid was found to have most potent analgesic activity with highest percentage protection. Selected compounds were also tested for their ulcerogenic potential and in vitro hydrolysis pattern in phosphate buffer pH 7.4 and acetate buffers of pH 3.0, 4.0, and 5.0, respectively. From the experimental data of present study, it has been concluded that these newly synthesized prodrugs of naproxen showed good analgesic activity with reduced or negligible ulcerogenic potential when compared to their parent drug.
SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL ANALOGS AMIDST SUBSTITUTED-2-AMINOBNZO-THIAZOLE AND 1,3,4-OXADIAZOLE-2-THIONE

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Despite several attempts to develop new structural prototype in search for more effective therapeutic agents, benzothiazole is still considered as one of the most versatile classical agent which have been extensively investigated for years and received the foremost attention of medicinal chemists worldwide due to their broad spectrum of biological significance as an anti-tumour, anti-tubercular, anti-malarial, anti-convulsant, anthelmintic, analgesic, anti-inflammatory, anti-diabetic etc. Thus, keeping in view the immense potentiality, it became the preferred choice for further molecular modification and exploration. Among various analogs of benzothiazole, 2-substituted derivatives have emerged as lead nuclei against microbial infections. In the present communication, it was envisaged that molecule possessing the above nuclei could be of advantage to synthesize novel entities that may be value in designing potent, selective and less toxic antibacterial agents. We report herein, the synthesis and antibacterial evaluation of some novel structural hybrids utilizing thio, methylene and aceto bridge between 6-substituted-2-aminobenzothiazole and 5-(pyridin-4-yl)-1,3,4-oxadiazole-2-thione. Linkers were selected on basis of bioisosteric approach. All the titled compounds were synthesized by using an appropriate synthetic route and characterized by using various spectral techniques (Mass, IR, 1H NMR etc). The antibacterial activities of all the synthesized compounds were evaluated against identifiable bacterial strains. Most of the titled compounds exhibited better activity than the standard compound against selected strains. Furthermore, compounds were also screened for antioxidant and analgesic effect, of which some compounds displayed good nociceptive and free radical scavenging activity.

POSTER PRESENTATION

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SYNTHESIS AND ANTHELMINTIC EVALUATION OF SOME NOVEL FLUOROQUINOLONES WITH ANTIMICROBIAL POTENTIAL

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A series of novel fluoroquinolone derivatives was synthesized by clubbing fluoroquinolone with thiadiazoles via acetamide linkage. The cyclodehydration of aryl carboxylic acids and thiosemicarbazide was carried out to form 2-amino-5-aryl-1,3,4-thiadiazoles, which on condensation with chloroacetyl chloride in dimethylformamide (DMF) as a solvent yielded 2-(2-chloroacetyl amino)-substituted thiadiazole derivatives. These derivatives were then clubbed with different fluoroquinolones in presence of DMF and sodium bicarbonate and five final compounds were obtained by recrystallization from DMF-water. These synthesized compounds were evaluated for their anthelmintic activity against Eisemia foetida. The major findings indicated that all of the synthesized compounds exhibited promising anthelmintic activity but among all, 1-ethyl-6-fluoro-7-(4-{2-[5-(4-nitro-phenyl)-1,3,4-thiadiazol-2-yl]amino)-acetyl]-piperazin-1-yl)-4-oxo-1,4-dihydroquinolione-3-carboxylic acid was found to be most potent anthelmintic agent with a mean paralyzing time of 23.60±0.67(p<0.01) and a mean death time of 39.20±1.15(p<0.01) when compared with the standard piperazine citrate, with a mean paralyzing time of 24.40±1.03 and a mean death time of 34.80±1.02 at a concentration of 200 mg/mL. Results of investigation suggested that fluoroquinolone derivatives substituted with chloro and dimethoxy group at thiadiazole ring were more potent anthelmintic agent than other derivatives.

POSTER PRESENTATION
ANTICANCER ACTIVITY PROFILE OF THIAZOLIDINONE DERIVATIVES

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Cancer is one of the most pernicious diseases which led to a large number of deaths worldwide. Limited efficacy of the current chemotherapy and its adverse effects led to the need for development of new anticancer agents. Thiazolidinone moiety is one of the most popular heterocyclic scaffolds depicting anticancer activity and these agents have occupied a vital position in the field of modern medicinal chemistry. A large number of studies were performed on thiazolidinones and their analogs for anticancer activities. This study includes the description of the recent advancements in a number of newly synthesized thiazolidinone derivatives which may provide a route for the development of new anticancer agents. In this paper, some new derivatives with promising anticancer activity are described.
NEW THIADIAZOLE DERIVATIVES AS POSSIBLE HYDROGEN PEROXIDE SCAVENGING AGENTS

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A series of new 2,5-disubstituted-1,3,4-thiadiazole derivatives has been prepared in the present investigation. Structures of the newly synthesized compounds were confirmed by suitable spectroscopic methods such as IR, NMR. All compounds were evaluated for their antioxidant activity by using standard protocol i.e. hydrogen peroxide (H₂O₂) scavenging method. The results revealed that most of the compounds showed high or moderate hydrogen peroxide scavenging activity. Among the synthesized compounds in this series, compound 5c (N-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)-6-methylbenzo[d]thiazol-2-amine was found to exhibit most significant antioxidant activity with percentage scavenging of 55.13% at 500 µg.
AN EFFICIENT AND ENVIRONMENTALLY BENIGN SYNTHESIS OF DIHYDROPYRIMIDONES

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Multicomponent coupling reactions (MCR) represent a highly valuable synthetic tool for the construction of novel complex molecular structure with single synthetic step. These types of reactions have some advantages over conventional linear syntheses, including lower costs, shorter reaction times, high degrees of atom economy, the possibility for combinatorial surveying of structural variations, and environmental friendliness. The dihydropyrimidone ring is an essential building block for numerous synthetic pharmaceuticals, and a wide variety of biologically active compounds. As a consequence, the development of general methods for the synthesis of dihydropyrimidone derivatives has been the subject of considerable synthetic efforts and still requires attention. Most current procedures either require costly and environmentally hazardous catalysts or harsh reaction conditions and involve low yielding reaction sequences. Keeping in view the importance of these biologically active compounds, a highly atom-economic one pot synthesis of functionalized dihydropyrimidone by a multicomponent condensation reaction of beta-keto ester, aldehyde and urea is reported in moderate to good yields at reflux.
Molecular modeling is a collection of (computer based) techniques for deriving, representing and manipulating the structures and reactions of molecules, and those properties that are dependent on these three dimensional structures. Molecular modeling described software for the visualization of molecular structures, over the past two decades term molecular modeling has expanded to include visualizing two and three dimensional structures, organizing many compound and their properties into data bases providing tools for analyzing molecular properties. Molecular modeling is essential tool to medicinal chemist in drug design. It generally plays important role in drug discovery process. This techniques aims to introduce in a simple way the hierarchy of computational modeling methods used nowadays as standard tools by organic chemists for searching for, rationalizing and predicting structure and reactivity of organic, bio-organic and organometallic molecules. The emphasis will be on helping to develop a feel for the correct ‘tool’ to use in the context of a typical problem in structure, activity or reactivity, by describing the limitations and strengths of each method. The techniques described include molecular visualization, equilibrium and transition state geometry location, molecular mechanics methods, semi-empirical, density functional molecular orbital methods, and methods for topological analysis of wave functions.
Drug Discovery and Development

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Drug discovery process is a critical issue in the pharmaceutical industry since it is a very cost-effective and time consuming process to produce new drug potentials and enlarge the scope of diseases incurred. Drug target identification, being the first phase in drug discovery is becoming an overly time consuming process. Drug discovery process operates on a target-based approach, in which the organism is seen as a series of genes and pathways and the goal is to develop drugs that affect only one gene or molecular mechanism (that is, the target) in order to selectively treat the deficit causing the disease without producing side effects. The stages of modern drug discovery process pipeline to find out the new drugs. Modern drug discovery process pipeline consists of seven important steps: target identification, target validation, hit and lead identification, lead optimization, pre clinical testing, chemical testing and new drug application (NDA) and food and drug administration (FDA) approval. The process of drug discovery involves the identification of candidates, synthesis, characterization, screening and assays for therapeutic efficacy. Once a compound has shown its value in these tests, it will begin the process of drug development prior to clinical trials.

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MEDICINAL IMPORTANCE OF PYRAZOLONE DERIVATIVES

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Scientific research programs and reports are continuously pouring in with respect to improvised synthetic techniques to prepare numerous pyrazolone derivatives with regard to their diverse biological, pharmacological and chemical applications. When pyrazolones were discovered, they were only known as NSAID but in recent times, they are known to exhibit antioxidant, anticancer, antibacterial and several other pharmacological actions. These derivatives were withdrawn from the market because of their adverse effects such as agranulocytosis, skin rashes and blood dyscrasia etc, but recently they are again finding their place in the market and are being extensively used in cerebral ischemia and cardiovascular diseases. Since its introduction into medicine, there have been more than 1000 compounds made in an effort to find others with more potent analgesic action combined with less toxicity. Keeping in view the increasing importance of these derivatives, a need for the review is felt. This review deals with up to date literature on biological and pharmacological properties of pyrazolone derivatives.
SYNTHESIS AND ANTIMICROBIAL SCREENING OF SOME NOVEL PHENOXYACETIC ACID DERIVATIVES

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Phenoxy acetic acid analogs are well known for their wide spectrum of bioactivities. Keeping in view the therapeutic potential of phenoxy acetic acids as well as taking advantage of biodegradability and biocompatibility of amino acids and peptides, an attempt was made toward the synthesis of a novel series of 2,6 dibromo-4-nitro phenoxyacetic acid analogs of aminoacids, dipeptides, and tripeptides using diisopropylcarbodiimide/dicyclohexylcarbodiimide (DIPC/DCC) as coupling agents and N-methylmorpholine (NMM) and triethylamine (TEA) as bases. Selected phenoxyacetyl peptides were further hydrolyzed using lithium hydroxide to get corresponding acid derivatives 3i and 3ii. Structure elucidation of all the newly synthesized compounds was done by elemental analysis and IR, ¹H NMR, ¹³C NMR and mass spectral data. The antibacterial and antifungal studies were performed against eight pathogenic bacteria and fungi. Among synthesized phenoxyacetic peptides, 1ii a and 1iii were found to be effective toward B. subtilis and S. epidermidis. In addition, compounds 2ii, 2iv and 3ii displayed potent antifungal activity against pathogenic Candida albicans.