

Excellence in Research work of which claimed for SUN Pharma Research Award-2023

1. We are currently using the Debus-Radziszewski multicomponent synthesis reaction to synthesize two sets of 2,4,5-tri- and 1,2,4,5-tetra-substituted (4a–4d) and 6a–6d) imidazole derivatives in our cascading effort to create new, powerful compounds. The obtained compounds confirm their structures were interpreted by $^1\text{H}/^{13}\text{C}$ NMR, FT-IR, elemental analysis, purity, and HPLC examination of the retention time. We have synthesized various imidazole derivatives based on the molecular docking studies for their binding affinities, wherein chemical 6c has demonstrated greater anti-proliferative action by producing higher rate of apoptosis than the other chemicals, supporting the *in-silico* prediction. By a single XRD study, the crystalline of compound 4d has been established. The triple negative breast cancer cell line (MDA-MB-221) was used to test the synthesized compounds for their *in vitro* anti-cancer effects. Results from oral squamous cell carcinoma cell line (H357) and pancreatic cancer cell lines (MIA PaCa-2) suggested that each substance, at different times, suppressed cell growth in a concentration-dependent manner. The *S. aureus* bacterial strain was found to be susceptible to compounds 4b and 6d, but only with a MIC of 12.5 $\mu\text{g/mL}$, compound 4d fairly inhibited the fungus *T. rubrum*. Research of molecular docking demonstrates effective interaction of the synthetic chemicals with the oncogenesis-related target known as MELK elevated binding profiles. The thorough molecular dynamics analysis was used to further examine the lead molecule 6c make sure the system is stable. Cited by Monalisa Mahapatra, Priyanka Mohapatra, Kakarla Pakeeraiah, Ravi Kumar Bandaru,, **Sudhir Kumar Paidesetty** “*In-vitro* anticancer evaluation of newly designed and characterized tri/tetra-substituted imidazole congeners- Maternal Embryonic Leucine Zipper Kinase inhibitors: molecular docking and MD Simulation approaches” ***International Journal of Biological Macromolecules* 249 (2023) 126084 SCI Impact factor 8.87**
<https://doi.org/10.1016/j.ijbiomac.2023.126084>
2. A series of *N*-heteroaryl- 4-(1-(2-oxo-2 H -chromen-3-yl) ethylideneamino) benzenesulfonamide (5a- 5h) have been produced by the condensation reaction of suitable N -heteroaryl- 4-amino benzenesul- fonamide (4a-4f) with derivatives of 3-acetyl coumarin (3a-3b) in ethanol. By using techniques like $^1\text{H}/^{13}\text{C}$ NMR, FTIR, HRMS, and elemental analysis, as well as XRD, the structures of these congeners were verified. Additionally, the antimicrobial assay findings for compounds 5a, 5d, and 5f showed that they were effective against the terbinafine-resistant *Trichophyton rubrum* when compared to ketoconazole, with an acceptable MIC value of 12.5 $\mu\text{g/}$

mL. Additionally, as compared to Gentamicin, compound 5f had the largest zone of inhibition against *Staphylococcus aureus*. Prior to molecular docking utilizing AutoDock4.2 and other concomitant settings, the generated hybrid molecules were examined and adjusted. The docking results of compounds 5d, 5e, 5f, and 5h with the cancer-causing protein showed binding energies in an ascending series of -9.28, -10.08, -11.88, and -12.4 Kcal/mol, which further motivated the evaluation of in vitro anticancer activity. The findings of screening the synthesized molecules against the MDA-MB-231, MIA PaCa-2, and H357 cancer cell lines showed that all of the compounds suppressed the proliferation of the cancer cells in a concentration-dependent way at various time points. Cited by Monalisa Mahapatra, Priyanka Mohapatra,, **Sudhir Kumar Paidesetty** “Design, synthesis, and in-silico study of chromen-sulfonamide congeners as potent anticancer and antimicrobial agents” *Journal of Molecular Structure*, 1283, (2023), 135190 **SCI Impact factor 3.86** <https://doi.org/10.1016/j.molstruc.2023.135190>

3. Due to a number of intrinsic factors, including resistance to antibacterials acquired through bacterial consortia, and extrinsic factors, including non-uniform antibacterial policy and the migration of resistant bacteria through human and other routes, bacterial multidrug resistance has recently become a common issue in clinics. Clinics are eagerly awaiting the creation of newer, more potent anti-mycobacterial candidates. Hybrid molecules might be more effective than conventional molecules in fighting invasive bacterial strains, but newer antibiotics are always being developed. Here, two series of Schiff-based salicylaldehyde S1–S7 and furfuraldehyde F1–F7 molecules, each having a sulfonamide group, are designed and developed. These compounds were synthesized, and their structures were validated by spectrum characterization. Simulated molecular dynamics of all atoms had been carried out concurrently to understand the mechanism of action with these leading complexes. These data imply that the synthesized Schiff-based salicylaldehyde hybrids would be promising anti-tubercular compounds, which further need potent pharmacological evaluations. Cited by Chita Ranjan Sahoo , **Sudhir Kumar Paidesetty** , Budheswar Dehury , Rabindra Nath Padhy “Computational study on schiff base derived salicylaldehyde and furfuraldehyde derivatives as potent anti-tubercular agents: Prospect to dihydropteroate synthase inhibitors” *Journal of Biomolecular Structure and Dynamics*, 2023, **SCI Impact factor 5.23** [10.1080/07391102.2023.2217918](https://doi.org/10.1080/07391102.2023.2217918)
4. It has been decades in the making, but antibiotic-resistant bacteria and fungus are suddenly becoming a potential worldwide public health emergency. In order to combat incidents of

antibiotic resistance, fresh, more effective medication options are urgently needed. A new series of p-cuminal sulfonamide Schiff base congeners 3a-3h were devised, synthesized, and had their structures verified by numerous spectral analyses in an effort to combat the issues with antimicrobial multi-drug resistance. *Staphylococcus aureus*, *Streptococcus pyogenes*, Methicillin-resistant *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and pathogenic fungi *Candida tropicalis* and *Trichophyton rubrum* were tested for the antimicrobial activities of the obtained products. With a MIC of 3.12 µg/mL, compound 3b significantly inhibited all strains of bacteria, and compound 3e showed the greatest amount of inhibition. In comparison to Ketoconazole, compound 3e showed the most promising control of both *C. tropicalis* and *T. rubrum* (MIC 6.25 µg/mL), as well as good inhibition of both *S. aureus* and MRSA at MIC 6.25 µg/mL. Sulfamoyl, azomethine, and certain heteroaryl rings in specific compounds may have enhanced their antibacterial effects, while the presence of guanyl and acetyl groups in the chemical structure may have contributed to their antifungal effects. Furthermore, biological targets have been determined for in silico research and drug-likeness. Cited by A K Bishoyi, M Mahapatra, **SK Paidesetty**, RN Padhy” Design, molecular docking and antimicrobial assessment of newly synthesized p-cuminal-sulfonamide Schiff base derivatives” *Journal of Molecular Structure*, 2022, 1250 131824, [10.1016/j.molstruc.2021.131824](https://doi.org/10.1016/j.molstruc.2021.131824) , Elsevier: **SCI Impact factor 3.86**

5. According to the World Health Organisation, breast cancer is currently the most common type of cancer. The most lethal subtype of breast cancer is triple negative, which is characterised by a high rate of metastasis and a dismal prognosis due to the absence of progesterone, oestrogen, and HER-2 receptors, three crucial therapeutic targets. In 45-70% of infected patients, this lethal variety shows overexpression of the epidermal growth factor receptor. The current study investigates a method to produce gold nanoparticles conjugated to flavonoids (luteolin) that may be easily and quickly synthesised with the aid of ultrasonication. The TEM measurements of the synthesised nanoparticles revealed a diameter of 30.23 ± 9.96 nm and good stability, as shown by zeta potential of 38.1 ± 1.49 mV. In UV-Vis spectroscopy, the particles displayed a distinctive plasmonic resonance at 541 nm. sphere-shaped particles. Spherical particles with face centered cubic crystalline structure were observed through HR-TEM, SAED and XRD analysis. In MDA-MB-231 TNBC cells, synthesised nanoparticles significantly increased cytotoxicity (IC₅₀ value of 2 µg/mL). Confocal imaging demonstrated that targeted nanoparticles quickly localised in the

nucleus of cancer cells, improving its effectiveness. Evaluations of the cell cycle and apoptosis revealed that after an increase of MDA-MB-231 cells in the sub-G1 phase, both necrotic and apoptotic cell death occurred. It's interesting to note that NIH-3T3 cells, which are not cancerous, were cytocompatible with nanoparticles, confirming their therapeutic promise as a biosafe formulation. The study presents the first report of targeted therapies for triple-negative breast cancer using biosafe gold nanoparticles conjugated to luteolin. Cited by Suvadeep Mal, Tiyasa Saha, Asim Halder, **Sudhir Kumar Paidesetty**,, Partha Roy "EGF-conjugated bio-safe luteolin gold nanoparticles induce cellular toxicity and cell death mediated by site-specific rapid uptake in human triple negative breast cancer cells" *Journal of drug and delivery system and technology* 80 (2023), 104148 SCI Impact factor 5.26 <https://doi.org/10.1016/j.jddst.2022.104148>.

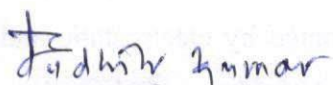
6. Even after being treated with ongoing multidrug therapy (MDT), leprosy remains a dangerous public health risk for the cause of severe impairment and final morbidity cases with stable prevalence rates. More unlucky individuals in some poor nations now fear leprosy as a result of dapsone (DDS) resistance. Here, using an azo-coupling procedure, DDS was chemically coupled with four different phytochemicals to create dapsone-phytochemical conjugates (DPCs). Before chemical synthesis and spectrum characterizations such as proton-HNMR, FTIR, UV, and LC-MS, possible biological activities were verified with computational chemistry and quantum mechanics via a molecular dynamics simulation programme. with the "mouse-foot-pad propagation method" and the active ingredient's host-toxicity testing, the in vivo antileprosy activity was seen with the WHO-recommended concentration of 0.01% mg/kg each DPC for 12 weeks. The DPC4 reduced one-log bacilli cells in the footpads of DDS-resistant sick mice while leaving no bacilli in the hind pads of DDS-sensitive mice. Since a small percentage of dead cells were discovered under a fluorescent microscope to be red, the in vitro host toxicity investigation also confirmed that the DCP4 up to 5,000 mg/L level was safe for oral administration. Locating the prospective chemical entity could be aided by a number of cutting-edge bioinformatics techniques, saving time and resources for in vitro and in vitro studies. According to research on in vitro host toxicity and in vivo antileprosy activity, DPC4 could be employed in MDT in place of DDS. Cited by Swain, S.S., **Paidesetty, S.K.**, Dehury, B., ...Vedithi, S.C., Padhy, R.N. "Computer-aided synthesis of dapsone-phytochemical conjugates against dapsone-resistant

Mycobacterium leprae” *Scientific Reports*, 2020, 10(1), 6839 [10.1038/s41598-020-63913-9](https://doi.org/10.1038/s41598-020-63913-9)

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7. The discovery of new UTI antibacterial agent(s) remains the order of the day given the prevalence of bacterial UTI (Urinary Tract Infection) around the world. Here, two series of 4-hydroxy coumarin derivatives based on Mannich, **7a-m** and **8a-m**, were created by condensing appropriate heterocyclic amines with aldehydes. In vitro antibacterial tests and ¹H- and ¹³C-NMR spectrum analysis were used to analyse the synthesised compounds. With MIC values of 12.50 and 25 mM, respectively, the substance 4-hydroxy-3-((4-hydroxy-3-methoxyphenyl)(morpholino)methyl)-2H-chromen-2-one **8l** was the major derivative against harmful bacteria *Staphylococcus aureus* and *Escherichia coli*. The analogues **7f**, **7l**, **8d**, **8j**, and **8k** could be effective druggable compounds with considerable binding affinity towards bacterial tyrosine kinase, as target, according to computational assessments utilising the Lipinski's rule of five, ADMET characteristics, and molecular docking studies. Each system was subjected to molecular dynamics simulations for 100 ns in order to understand the manner of binding and intrinsic stabilities of powerful receptor-ligand complexes. The analogues **8l** form a variety of non-bonded interactions, according to intermolecular contact studies and inherent hydrogen-bond stability, while the receptor tyrosine kinase is primarily dominated by electrostatic and hydrophobic contacts. The outcomes of the current structure-based designing technique may prove to be a useful tool in the near future for the discovery of new antibacterial medication candidate(s) against UTI. Cited by Sahoo, C.R., **Paidesetty, S.K.**, Dehury, B., Padhy, R.N. “Molecular dynamics and computational study of Mannich-based coumarin derivatives: potent tyrosine kinase inhibitor” *Journal of Biomolecular Structure and Dynamics*, 2020, 38(18), 5419. 5428, [10.1080/07391102.2019.1701554](https://doi.org/10.1080/07391102.2019.1701554) Taylor & Francis **SCI Impact factor 5.26**
8. Antibiotic resistance has been building for years and is finally manifesting itself as a major global public health problem. As a result, there is an urgent need for novel, more powerful medication candidates to combat the anticipated rise of antibiotic-resistant bacteria and fungi. The Mannich condensation synthesis of the corresponding cyclic amines **3a-3g** and N-heteroaryl-4-amino benzenesulfonamide **3h-3l** with thymol and formaldehyde in an acidic medium was devised and used to create a series of amino methylated sulfonamide congeners, **4a-4l**, that contain thymol. By performing spectroscopic analyses, including ¹H/¹³C NMR, FTIR, ESI-HRMS, and elemental analysis, the structures of the synthesised compounds were confirmed. XRD analysis was used

to characterise the powder of the synthesised compounds. *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Escherichia coli*, as well as *Candida*, were used to test the derived compounds' antibacterial and antifungal properties. All compounds' antimicrobial activities showed moderate to excellent bacterial inhibition, but 2-isopropyl-5-methyl-4-(pyrrolidin-1-ylmethyl)phenol, 4f, significantly inhibited *S. aureus* and *E. coli* with MICs of 3.12 g/ml and 12.5, respectively. With a MIC of 6.25 g/ml for *E. coli* and *S. aureus* and 3.12 g/ml for *T. rubrum*, the compound 4-((dimethylamino)methyl)-2-isopropyl-5-methylphenol, 4 g, showed good inhibition. The synthetic chemicals 4g and 4h inhibited the fungus *T. rubrum* with the maximum levels at 27 and 28 mm, respectively. As a result, the synthetic compounds containing methylated dimethylamino in thymol may be the best candidates for having antibacterial and antifungal effects. Cited by AK Bishoyi, M Mahapatra, **SK Paidesetty**, RN Padhy "Design, molecular docking, and antimicrobial assessment of newly synthesized phytochemical thymol Mannich base derivatives" *Journal of Molecular Structure*, 2021, 1244, 130908 [10.1016/j.molstruc.2021.130908](https://doi.org/10.1016/j.molstruc.2021.130908) Elsevier **SCI Impact factor 3.86**



Dr. P Sudhir Kumar

Professor

School of Pharmaceutical Sciences

Siksha 'O' Anusandhan

(Deemed to be University)

Google scholar h-index-21

Scopus ID-57189328087

<https://orcid.org/0000-0003-1210-2293>