Ten Best Papers of Professor Diwan S Rawat

1. Synthesis of novel monocarbonyl curcuminoids, evaluation of their efficacy against MRSA, including ex vivo infection model and their mechanistic studies, Gagandeep, Prince Kumar, Shamseer Kulangara Kandi, Kasturi Mukhopadhyay, **Diwan S. Rawat***, **Eur. J. Med. Chem. 195, 112276 (2020).** ***Impact Factor:*** **5.572.**

   Summary: A series of novel monocarbonyl curcuminoids were synthesized and these compounds showed potent antibacterial activity against both methicillin-sensitive and methicillin-resistant strains of *S. aureus* with MIC values 2-8 and 4-16 mg/mL, respectively. They also exhibited moderate potency against *E. coli* strains. And these compounds were non-hemolytic, and non-toxic toward mammalian cells up to 150 mg/mL concentration. Mechanistic studies revealed that these curcuminoids displayed potent bactericidal activity by targeting cell membranes. In an *ex vivo* mammalian co-culture infection model study, two of the compounds were able to clear the internalized bacteria in mammalian cells and the activity was found to be superior to conventional antibiotics such as vancomycin and linezolid. These water soluble, non-toxic curcuminoids may serve as a lead molecule for development as antibacterial agents against MRSA infections.

2. Hybridization of fluoro-amodiaquine (FAQ) with pyrimidines: Synthesis, *in vitro* and *in vivo* antimalarial potency of FAQ-pyrimidines; Mohit Tripathi, Dale Taylor, Shabana I. Khan, Babu L. Tekwani, Prija Ponnan, Thirumurthy Velpandian, Ujjalkumar Das, **Diwan S. Rawat*** **ACS Med. Chem. Lett.** 10, 714–719 **(2019), Impact factor: 3.975. Citation: 15**

   Summary: To evade the possible toxicity associated with the formation of quinone-imine metabolite in amodiaquine (AQ), the para –hydroxyl group was replaced with a –F atom and the resulting 4'-fluoro-amodiaquine (FAQ) was hybridized with substituted pyrimidines. The synthesized FAQ-pyrimidines displayed better in vitro potency than chloroquine (CQ) against the resistant P. falciparum strain (Dd2), exhibiting up to 47.3-fold better activity (IC_{50}: 4.69 nM) than CQ (IC_{50}: 222 nM) and 2.8-fold better potency than artesunate (IC_{50}: 13.0 nM). Twelve compounds exhibited better antiplasmodial activity than CQ against the CQ-sensitive (NF54) strain. Two compounds were evaluated in vivo against a P. berghei-mouse malaria model and displayed better activity than CQ and comparable to AQ at 33.3 mg/Kg dose. Mechanistic heme-binding studies and computational docking against Pf-DHFR was performed for the best molecules of the series to correlate their high antiplasmodial activities.

3. Novel 4-aminoquinoline-pyrimidine based hybrids with improved *in vitro* and *in vivo* antimalarial activity, Sunny Manohar, U. Chinna Rajesh, Shabana I. Khan, Babu L. Tekwani, **Diwan S. Rawat***, **ACS Med. Chem. Lett.** 3, 555-559 **(2012). Impact factor: 3.975. Citations: 131**

Summary: A class of hybrid molecules consisting of 4-aminoquinoline and pyrimidine were synthesized and tested for antimalarial activity against both chloroquine (CQ)-sensitive (D6) and chloroquine (CQ)-resistant (W2) strains of Plasmodium falciparum through an in vitro assay. Eleven hybrids showed better antimalarial activity against both CQ-sensitive and CQ-resistant strains of P. falciparum in comparison to standard drug CQ. Four molecules were more potent (7-8 fold) than CQ in D6 strain and eight molecules were found to be 5-25 fold more active against resistant strain (W2). Several compounds did not show any cytotoxicity up to a high concentration (60 μM), others exhibited mild toxicities but the selective index for the antimalarial activity was very high for most of these hybrids. Two compounds selected for in vivo evaluation have shown excellent activity (p.o.) in a mouse model of P. berghei without any apparent toxicity. X-ray crystal structure of one of the compound was also determined.

Molecule has been taken up by NURRON Pharmaceuticals, Boston for development as anti-Parkinson drug.

4. Deepak Kumar, Beena, Garima Khare, Saqib Kidwai, Anil K. Tyagi, Ramandeep Singh, **Diwan S Rawat***, Synthesis of novel 1,2,3-triazole derivatives of isoniazid and their *in vitro* and *in vivo* antimycobacterial activity evaluation, **Eur. J. Med Chem.** 81, 301 – 313 (**2014**). ***Impact Factor:*** **5.572, Citation: 81**

Summary: A molecular hybrids consisting of isoniazid and 1,2,3-triazoles were synthesized and evaluated for antimycobacterial activity. Most of the compounds exhibited potent activity against *Mycobacterium tuberculosis* H37Rv strain with MIC_{99} values ranging from 0.195 to 1.56 μM *in vitro*. One compound showed better *in vitro* activity than the reference, whereas five compounds were equally potent to the reference compound isoniazid without any observed toxicity even at 50 μM concentration. *In vivo* activity of the best compound in murine model of tuberculosis significantly reduced bacillary load in both lungs and spleen at 10 weeks post-treatment.

5. U. Chinna Rajesh, Jinfeng Wang, Stuart Prescott, Takuya Tsuzuki, **Diwan S. Rawat***, RGO/ZnO nanocomposite: An efficient sustainable heterogeneous amphiphilic catalyst for the synthesis of 3-substituted indoles in water. **ACS Sustainable Chem. Eng.** 3, 9 – 18 (**2015**) **[Highlighted in the Cover Page]. Impact Factor: 8.198. Citation: 106.**

Summary: A nanocomposite consisting of reduced graphene oxide and zinc oxide nanoparticles (RGO/ZnO) with unique structural features was developed as a highly efficient reusable heterogeneous amphiphilic catalyst for the synthesis of various 3-substituted indoles in aqueous medium. The catalyst was recycled six times without significant loss of the catalytic activity. The higher environmental compatibility and sustainability factor such as smaller E-factor and higher atom economy makes the present methodology a true green process for the synthesis of biologically important 3-substituted indoles.

6. U. Chinna Rajesh, Sunny Manohar, **Diwan S Rawat***, Hydromagnesite as an efficient novel recyclable heterogeneous solid base catalyst for the synthesis of

flavanones, flavanols and 1,4-dihydropyridines in water. **Adv. Synth. Catal.** 355, 3170 – 3178 (**2013**). **Impact Factor: 5.45; Citation: 46.**

Summary: Flower like thin sheet morphology of hydromagnesite (HM) was synthesized by environmentally benign approach using simple conventional heating at low temperature without using any template in water medium. The versatility of HM catalyst was studied in the synthesis of flavanones, flavanols and multicomponent synthesis of 1,4-dihydropyridines in water. The recyclability of catalyst was studied for six times and there was no appreciable loss in its catalytic activity.

7. U. Chinna Rajesh, Gunjan Purohit, **Diwan S. Rawat*** Facile one-pot synthesis of N-heterocycles using CuI/CSP composites as efficient recyclable nanocatalysts with anomalous selectivity under green conditions, **ACS Sustainable Chem. Eng.** 3, 2397 – 2404 (**2015**). **Impact Factor: 8.198; Citation: 35**

Summary: CuI/CSP nanocomposites were developed as efficient and recyclable nanocatalysts for one-pot synthesis of aminoindolizines *via* A3 coupling reaction in the presence of ethylene glycol (EG) as a recyclable solvent. In contrast, chalcones were isolated when the reaction was performed in the presence of secondary amines such as piperidine, 3-methylpiperidine, pyrrolidine and piperazine under solvent free conditions. The CuI/CSP was recycled for five times without significant loss in its catalytic activity. The anomalous selectivity in the formation of aminoindolizines and chalcones was dependent of solvents and secondary amines used for the reaction. The present methodology is facile and follows green principles with higher atom economy (94%), smaller E-factor (0.06).

8. P. Linga Reddy, Mohit Tripathi, R. Arundhathi and **Diwan S. Rawat***, Chemoselective hydrazine-mediated transfer hydrogenation of nitroarenes by Co_3O_4 nanoparticles immobilized on a Al/Si-mixed oxide support, **Chemistry - An Asian Journal**, 12, 785 – 791 (**2017**). **Impact Factor: 4.592 [Highlighted by Synfacts 2017; 13(07): 0766]**. **Citation: 20**

Summary: Cobalt oxide nanoparticles impregnated on an alumina-silica (mixed oxide) were synthesized. The porous alumina-silica having a high surface area served as a protective heterogeneous support on which the well-dispersed Co_3O_4 nanoparticles served as an active catalyst species for the hydrazine-mediated transfer hydrogenation of nitroarenes and the catalytic system chemoselectively transfer-hydrogenate nitroarenes in the presence of other labile functional groups such as halide, alkene, nitrile, carbonyl, ester etc. This inexpensive catalyst was also able to catalyze gram scale reaction and was found to be robust and recyclable up to eight runs.

9. $Cp^*Co(CO)I_2$] Catalysed C—C bond formation and [2+2+2] annulation of 1,3-dicarbonyls to terminal alkynes, Girjesh Kumar Verma, Manish Rawat, **Diwan S. Rawat* Eur. J. Org. Chem.** 4101–4104 (**2019**). **Impact Factor: 3.029.**

Summary: A highly regioselective [$Cp^*Co(CO)I_2$] catalyzed addition of 1,3-diketones to terminal alkynes at room temperature have been achieved using $Cu(OTf)_2$ as a co-catalyst. Reaction of 1,3-diketones having substitution at active methylene carbon with phenyl acetylenes having electron withdrawing group or bulky group results in the formation of 2-alkenylated 1,3-dicarbonyl product, but phenyl acetylenes with electron donating group led to the formation of tetrahydronaphthalene and terphenyl.

10. N. Kumar, S. I. Khan, H. Atheaya, R. Mamgain, **Diwan S. Rawat*** "Synthesis and *in vitro* antimalarial activity of tetraoxane-amine/amide conjugates" **Eur. J. Med. Chem.** *46*, 2816-2827 **(2011). *Impact Factor:* 5.572, Citation: 48.**

Summary: A series of tetraoxanes, tetraoxane-amine and tetraoxane-amide conjugates has been synthesized and screened for *in vitro* antimalarial activity against chloroquine-sensitive and chloroquine-resistant strains of *P. falciparum*. Most of the conjugates showed enhanced antimalarial activity than the parent tetraoxanes. Three of the conjugate compounds were potentially active with IC_{50} values in the range of 0.38 to 0.80 μM. Cytotoxicity of four selected compounds was also evaluated in a panel of four cancer (SK-MEL, KB, BT-549, SK-OV-3) and two non-cancer (Vero and LLC-PK_{11}) cell lines up to a concentration of 25 μM and none of the compounds was found toxic to any of the cells.