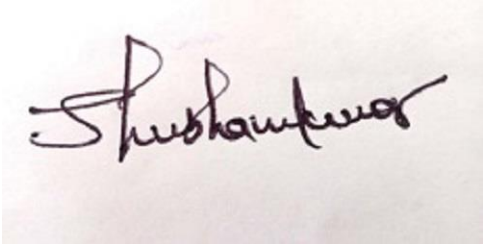
List of Publications

1. Arora N, Dhiman P, **Kumar S**, Singh G, Monga V. Recent Advances in Synthesis and Medicinal Chemistry of Benzodiazepines. *Bioorg Chem*. 2020; 97:103668. doi:10.1016/j.bioorg.2020.103668. (IF = 5.275)
2. **Kumar S**, Khatik GL, Mittal A."Recent Developments in Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors as a Valuable Tool in the Treatment of Type 2 Diabetes Mellitus", *Mini Rev. in Med. Chem*. 2020;20(3):170-182. doi:https://doi.org/10.2174/1389557. (IF = 3.862)
3. **Kumar S**, Khatik GL, Mittal A. In-silico Molecular Docking Study to Search New SGLT2 Inhibitor based on Dioxabicyclo[3.2.1] octane Scaffold. *Curr Comput Aided Drug Des*. 2020;16(2):145-154.. doi:10.2174/1573409914666181019165821. (IF = 1.606)
4. **Kumar S**, Rulhania S, Jaswal, S, Monga, V. 2020. Recent advances in the medicinal chemistry of carbonic anhydrase inhibitors. *Eur. J. Med. Chem.* p.112923. (IF = 6.51)
5. **Kumar S**, Mittal A, Babu D. Herbal medicines for diabetes management and its secondary complications. *Curr. Diabetes Rev*. 2020 Nov 3. (IF = 1.95)
6. Jaswal S, Nehra B, **Kumar S**, Monga V. Recent advancements in the medicinal chemistry of bacterial type II topoisomerase inhibitors. *Bioorg. Chem.*. 2020 Sep 3:104266. (IF = 5.275)
7. Sharma S, Mittal A, **Kumar S**. Structural Perspectives and Advancement of SGLT2 Inhibitors for the Treatment of Type 2 Diabetes. *Current Diabetes Reviews*. 2021 Sep 17. (IF = 1.95)
8. **Kumar S**, Mittal A, Mittal A. A review upon medicinal perspective and designing rationale of DPP-4 inhibitors. *Bioorg. Med. Chem.*;46:116354. (IF = 3.641)
9. Rulhania S, **Kumar S**, Nehra B, Gupta GD, Monga V. An insight into the medicinal perspective of synthetic analogs of imidazole. *J. Mol. Str.*. 2021 May;1232:129982. (IF =3.196)
10. Yadav A, **Kumar S**, Monga V. Progress in the Development of Potential Therapeutics and Vaccines against COVID-19 Pandemic, *Acta Scientific Pharmaceutical Sciences*. 2021, 5 (7), 45-62. (IF = 1.020).
11. **Kumar S**, Arora P, Wadhwa P, Kaur P. A Rationalized Approach to Design and Discover Novel Non-steroidal Derivatives through Computational Aid for the Treatment of Prostate Cancer. Curr Comput Aided Drug Des. 2023 Jun 26. doi: 10.2174/1573409919666230626113346. Epub ahead of print. PMID: 37365786.
12. Handa Jasmeen, Kumari Baby, Negi Samir, Arora Pinky and **Kumar Shubham***, Utilization of computational tools for discovery of reticuline based derivatives as AChES inhibitors to treat Alzheimer's disease, Letters in Drug Design & Discovery 2023; 20() . https://dx.doi.org/10.2174/1570180820666230713112757



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A review upon medicinal perspective and designing rationale of DPP-4 inhibitors

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is one of the highly prevalence disorder and increasing day by day world-widely. T2DM is a metabolic disorder, which is characterized by deficiency in insulin or resistance to insulin and thus increases the glucose levels in the blood. Various approaches are there to treat diabetes but still there is no cure for this disease. DPP-4 inhibitor is a privileged target in the field of drug discovery and provides various opportunities in exploring this target for development of molecules as antidiabetic agents. DPP-4 acts by inhibiting the incretin action and thus decreases the level of blood glucose by imparting minimal side effects. Sitagliptin, vildagliptin, linagliptin etc. are the different DPP-4 based drugs approved throughout the world for the treatment of diabetes mellitus. Cyanopyrrolidines, triazolopiperazine amide, pyrrolidines are basic core nucleus present in various DPP-4 inhibitors and has potential effects. In the past few years, researchers had applied various approaches to synthesize potent DPP-4 inhibitors as antidiabetic agent without side effects like weight gain, cardiovascular risks, retinopathy etc. This review will also emphasize the recent strategies and rationale utilized by researchers for the development of DPP-4 inhibitors. This review also reveals about the various other approaches like molecular modelling, ligand based drug designing, high throughput screening etc. are used by the various research group for the development of potential DPP-4 inhibitors.

1. Introduction

Diabetes Mellitus is one of the serious issues nowadays. Diabetes is a metabolic disorder which arise from a variety of pathogenic mechanisms. Diabetes is of two types: Type 1 Diabetes Mellitus (T1DM) which is also classified as Insulin Dependent Diabetes Mellitus (IDDM) and Type II Diabetes Mellitus (T2DM) classified as Non-Insulin Dependent Diabetes Mellitus (NIDDM)[1]. In T1DM, destruction of β-cells are caused by the autoimmune process, this lead to insulin deficiency and caused T1DM[2] whereas T2DM characterized by insulin resistance[3] and in this, β-cells produces insulin but body cells resist the normal effect of insulin or peripheral action of hormone is defected[4]. Diabetes mellitus is one of the most serious disease in the world and according the recent report of International Diabetes Federation (IDF), a total of 463 million people are having diabetes mellitus and will rise upto 578 million by 2030 and 700 million by 2045 whereas in South East Asia (India) a total of 74% of diabetes cases will increase by 2045[5]. Diabetes also gave rise to several other complications like cardiovascular disease[6], retinopathy, obesity[7], foot damage[8], nephropathy, neuropathy[9], alzheimer's disease[10], hearing impairment etc.[11]. Several approaches such as peroxisome proliferator-activated receptors (PPAR) agonists[12], sulfonyl urea, biguanides, α-glucosiadse inhibitors, thiazolidinediones, incretin mimetic, meglitinides, protein tyrosine phosphatase-1b (ptp1b) inhibitors[13], sodium glucose co transporter (SGLT-2) inhibitors[14],

Abbreviations: T2DM, Type 2 diabetes mellitus; DPP, dipeptidyl peptidase; FAP, fibroblast activation protein IDDM, insulin dependent diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; IDF, international diabetes federation; PPAR, peroxisome proliferator-activated receptors; SGLT, sodium glucose co transporter; DGAT, diacylglycerol acyltransferase; HSD, hydroxysteroid dehydrogenase; GLP, glucagon-like peptide; GFAT, glutamine fructose-6-phosphate amidotransferase; GLUT, glucose transporter type; MAP, mitogen activated protein; GSK, glycogen synthase kinase; GIP, glucose-dependent insulinotropic polypeptide; SPPS, solid phase peptide synthesis; SAR, structure activity relationship; SI, selectivity index; IC, inhibitory concentration; AUC, area under curve; PK, pharmacokinetics; OGTT, oral glucose tolerance test; nM, nanomolar; μM, micromolar; P.O, oral administration; I.V, intravenous.

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Recent advances in the medicinal chemistry of carbonic anhydrase inhibitors

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