ABSTRACT

In the pursuit of discovering new targets and disease specific drugs, 40% of the new chemical entities (NCEs) coming out of drug discovery groups at pharmaceutical companies are facing poor water solubility challenges and poor bioavailability. Combinatorial chemistry and high throughput screening pursued by pharmaceutical companies are intrinsically biased towards poorly aqueous soluble drugs. To identify “leads” from such discovery compounds with challenging pharmaceutical properties, various screens are adopted. Identifying the appropriate lead compounds and further formulating them optimally becomes the key, since the poor bioavailability is often cited as the reason for the discontinuation of development of new chemical entities.

The poor water solubility of the NCEs is caused by hydrophobicity, i.e., the inability to form hydrogen bonds with water and by high lattice energy. One market analysis report estimated that worldwide sales of about $37 billion of drugs were insoluble or poorly soluble. Find a promising molecule (a “lead compound”) that could become a drug armed with their understanding of the disease, scientists are searching for potent drugs. They search for a molecule, or “lead compound” that may act on their target to alter the disease course. If successful over long odds and years of testing, the lead compound can ultimately become a new medicine. High-throughput screening is the process by which the leads are usually found. Advances in robotics and computational power allow researchers to test thousands of compounds against the target to identify the one that might be promising. Based on the results, several lead compounds are usually selected for further study.

Sulfonamides are versatile drugs with the broad Spectrum of biological activities such as antiviral, antifungal, diuretics, antibacterial and anticancer activities.
In the present research work, 28 sulfonamide compounds have been synthesized.

The sulfonamides have been synthesized by reacting the amines such as, Phenylethylamine, 2-(3,4-Dimethoxyphenyl)-N-methylethanamine, 1-((4-Chlorophenyl)(phenyl)methyl)piperazine and N-(5-Bromo-2-chlorobenzyl)cyclopropanamine, which are active pharmaceutical intermediates, whose biological activity was partly studied with aromatic sulfonyl chlorides such as Benzenesulfonyl chloride, 4-Methylbenzene-1-sulfonyl chloride, 2,4-Dichlorobenzene-1-sulfonyl chloride, Naphthalene-1-sulfonyl chloride, Naphthalene-2-sulfonyl chloride, 4-Bromo-3-(chlorosulfonyl)-5-methylbenzoic acid and Quinoline-8-sulfonyl chloride.

The advantages of doing this type of research are:

1. Easy availability of raw materials.
2. Control over genotoxic impurities.
4. Good at crystallization studies.
5. Good for salt formation which makes it water soluble.
6. Easy to understand the drug metabolism.

The structures of all the compounds have been established by FTIR, $^1$H NMR, MASS and elemental analysis. The crystal pattern of four compounds has been solved by SHELXL-97 computer program. All the 28 compounds have been screened for in vitro anticancer activity against five cancer lines such as Panc1(Pancreas), ACNH(Renal), Calu 1 (Lung), HCT116 (Colon), H460 (Non Small Cell Lung) using High-throughput Screening technique. Out of 28 compounds, 4-Bromo-3-[(5-bromo-2-chloro-benzyl)-cyclopropyl-sulfamoyl]-5-methyl-benzoic acid and N-(5-bromo-2-chlorobenzyl)-N-cyclopropylquinoline-8-sulphonamide have shown good anticancer activity in all the five cancer cells taken for the study.