CHAPTER 5
CONCLUSION
CONCLUSIONS

In the present investigation, the substituted isoquinolone (JS1-JS20) and benzothiazine (JS21-JS40) were synthesised and evaluated for their pharmacological and anti-microbial studies. The results of the studies can be summarised as follows:

- The isoquinolone and benzothiazine were synthesised in appreciable yield (60-90%). The spectroscopic data (IR,\(^1\)HNMR, MS and C,H,N elemental analysis) of synthesised compounds were found in agreement with the assigned molecular structure. The synthesised compounds were evaluated for their anti-inflammatory, analgesic, anti-bacterial and anti-fungal activities.

- The anti-inflammatory studies by both acute (carrageenan induced rat paw edema) and chronic (cotton pellet induced granuloma) models indicated that 4-Methyl-N-(1-oxo-3,4-diphenyl-1H-isoquinolin-2-yl)-benzene sulphonamide JS13 and 2-(4-Chloro-benzenesulfonyl)-3,4-diphenyl-2H-isoquinolin-1-one JS20 from series 1 and N-(1,1-Dioxo-3,4-diphenyl-1H-1--benzo(e)(1,2)thiazin -2-yl)-4 methyl-benzenesulphonamide JS33 and 2-(4-Chloro-benzenesulfonyl)-3,4-diphenyl-2H-benzo(e)(1,2)thiazine 1,1-dioxide JS40 from series II are the most effective anti-inflammatory agent. The xylene induced topical anti-inflammatory activity indicated JS3, JS13 from series 1 and JS25 and JS33 from series 2 are the most effective topical anti-inflammatory agent.

- The peripheral analgesic activities of synthesised (JS1-JS40) were determined by acetic acid induced writhing method. The results of analgesic activity indicated that 4-Methyl-N-(1-oxo-3,4-diphenyl-1H-isoquinolin-2-yl)-benzene sulphonamide JS13 and 2-(4-Chloro-benzenesulfonyl)-3,4-diphenyl-2H-isoquinolin-1-one JS20 from series 1 from series 1 and N-(1,1- Dioxo-3,4- diphenyl-1H -1- benzo(e)(1,2) thiazin-2 -yl) -benzenesulphonamide 2H- 1,1-dioxide JS25, Furan-2-carboxylic acid(1,1-dioxo-3,4-diphenyl-1H-1 benzo (e)(1,2)thiazine-2-yl) amide JS27 and N-(1,1-Dioxo-3,4-diphenyl-1H-1--benzo(e)(1,2)thiazin -2-yl)-4 methyl-benzenesulphonamide JS33 from series 2 were the most effective compounds at the dose of 100mg/kg orally when compared to the reference standard Diclofenac at the dose of 100mg/kg orally.

- 4-Methyl-N-(1-oxo-3,4-diphenyl-1H-isoquinolin-2-yl)-benzene sulphonamide JS13 and 2-(4-Chloro-benzenesulfonyl)-3,4-diphenyl-2H-isoquinolin-1-one JS20 from series 1 and N-(1,1-Dioxo-3,4-diphenyl-1H-1--benzo(e)(1,2)thiazin -2-yl)-4 methyl-benzenesulphonamide JS33 and 2-(4-Chloro-benzenesulfonyl)-3,4-diphenyl-2H-
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*benzo(e)(1,2)thiazine 1,1-dioxide* JS40 from series 2 showed significant reduction in swelling in acute arthritis models upon oral administration and the compound may offer a promising way to stop the progression of rheumatoid arthritis.

- The histopathological studies after chronic inflammation studies for the most active compound 4-Methyl-N-(1-oxo-3,4-diphenyl-1H-isoquinolin-2-yl)-benzene sulphonamide JS13 from isoquinolone series and N-(1,1-Dioxo-3,4-diphenyl-1H-1--benzo(e)(1,2)thiazin -2-yl)-4 methyl-benzenesulphonamide JS33 from benzothiazine series showed normal myocardium and no signs of ulceration in stomach and normal liver.

- The result of antimicrobial studies by tube dilution method indicated compounds with sulphonamide group were the most active compounds amongst various isoquinolone and benzothiazine derivatives as evidenced by their MIC values.

- The Quantitative structure activity relationship (QSAR) studies were carried out to find out the correlation between the physicochemical characteristics and their biological activity. These indicated that:

  - The topological parameters $3\chi_v$ and $\mu$ were found effective in describing the anti-inflammatory and analgesic activity for benzothiazine series.

**Future Scope**

- Docking studies can be performed for the synthesised compounds.

- The compounds JS13 and JS33 can further be evaluated for chronic arthritis models.

- These compounds may be screened further for the detailed pharmacological, toxicological and clinical studies.