The present work pertains to the “Synthesis and Evaluation of some prodrugs for colon targeting”.

Prodrugs have become an established concept and a powerful tool in optimizing the pharmacologically potent structures and overcoming physicochemical, pharmaceutical and biopharmaceutical barriers to a drug's usefulness. Prodrugs can be used for several reasons e.g. to enhance poor aqueous solubility, permeability or chemical stability, to prolong the duration of drug action, to improve drug targeting, to reduce side-effects and too rapid elimination and to extend the patent protection of the parent drug. An ideal prodrug has optimal physicochemical properties, such as lipophilicity and solubility, it is stable in the GI-tract or in its desired dosage form, the promoiety is non-toxic and it releases the active drug at an appropriate site and rate in vivo. However, the application of prodrug is not limited to merely include the bioavailability and pharmacokinetic behaviour of the drug, but it extends to control and targeted drug deliveries. One of such target site is the colon.

Literature available in the field on colon targeting indicates the difficulty in treatment of IBDs which is a common symptom for all the diseases of colon, viz, crohn’s disease and colon cancer due to failure of the drug to reach the site of action i.e. colon in appropriate concentration because of their early absorption in upper gastro-intestinal tract. Prodrug approach is one of the most conventional concepts used for the treatment of such colonic diseases.

In the present project, it was envisaged to synthesize mutual prodrugs to deliver the drug effectively to colon without releasing and absorbed the drug at upper part of GIT. This concept will not only target the drug to colon but also avoid the release/absorption of drug at unwanted sites. This means that the various gastro-intestinal adverse effects will be avoided and as a result of increasing the molecular weight, the absorption of drug will be lesser due to very low water solubility.

In view of this context, mutual amide prodrugs of Norfloxacin and Trimethoprim with Aspirin (AN and AT); Norfloxacin and Trimethoprim with Indometacin (IN and IT) by Schotten-Baumann reaction followed by coupling; and mutual azo prodrugs of sulfadiazine and sulfamethoxazole with salicylic acid (SDS and SMS) by diazotization followed by coupling method were synthesized. The
physico-chemical properties of synthesized prodrugs were determined and their structures were supported and analyzed by FTIR, $^1$H NMR and Mass spectroscopy. *In vitro* release study of the synthesized derivatives was done in different simulated gastro-intestinal fluids to identify the expected hydrolysis of these amide and azo conjugates in gastrointestinal tract. All the conjugates were found chemically stable in simulated gastric fluid (SGF, pH 1.2) and simulated jejunal fluid (SJF, pH 4.5), implying that they did not undergo hydrolysis and would be stable in the acidic pH of stomach. To confirm the colonic hydrolysis of the synthesized prodrugs, further release studies in simulated colonic fluid (SCF, pH 7.0) incorporating with amidases, esterases and other enzymes indicates appreciable release of free drugs from the prodrugs.

Thus, anti-inflammatory action of NSAIDs can be capitalized and the antibacterial drug is also not absorbed due to their higher molecular weight from GIT. As a result the prodrug and released drugs remain in the GIT only. Abolition of unwanted absorption of drugs will lower the doses, thus increasing the therapeutic utilization of drugs. This more therapeutic utilization will reduce the cost of treatment and more importantly the adverse effects caused by the parent drugs will be abolished.