

## Development of Sulphasalazine a Follow through

### Sajith Sebsatian\*

Consultant Gastroenterologist, MGM Muthoot Hospital, Pathanamthitta, Kerala, India

\*Corresponding Author: Sajith Sebsatian, Consultant Gastroenterologist, MGM Muthoot Hospital, Pathanamthitta, Kerala, India.

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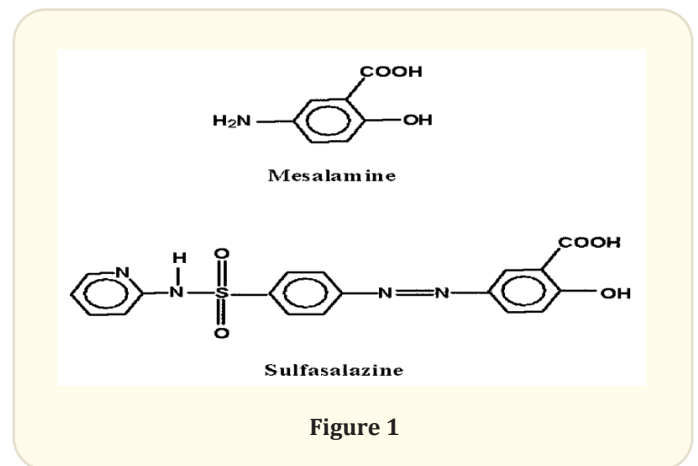
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It was professor Nana Svartz -1890-1986, Karolinska Institute, Stockholm, convinced that Rheumatic arthritis was caused by *Streptococci*. He later Hypothesised that combination with salicylic acid would deliver Sulfapyridine to affected joints. But it was only until late November 1940, when a 17yr old boy.

With chronic Arthritis and colitis for 5yr was treated with Sulfapyridine in hospital for 9 months and later followed by sulphasalazine. His Colitis responded rapidly and he improved within a few months and later discharged. It was then realised that colitis patients responded better than Rheumatic arthritis. This led to the usage of sulfa drugs in patients with colitis and arthritis during that time. Mesalamine, it was discovered as the active anti-inflammatory moiety of sulfasalazine, which has been used to treat ulcerative colitis since the late 1940s. Sulfasalazine contains mesalamine or 5-ASA bound to sulfapyridine via an azo bond. It is released by bacterial enzyme azo reductase present in the small bowel and colon. Sulfapyridine is inactive, but is absorbed in the colon and is mostly responsible for hypersensitivity reactions and adverse effects associated with sulfasalazine. It is then excreted in the urine as free 5-ASA and N-Ac-5-ASA. Most of the side effects of salazopyrine drugs were attributed due to Sulfapyridine. Mesalamine compared were absorbed rapidly from gut and pre-systemically acetylated. Relative systemic exposure is low. Overall, 30% of the unbound 5-ASA is then absorbed rapidly in the small intestine, metabolized locally and by the liver to N-Ac-5ASA (an inactive metabolite) by N-acetyltransferase 1 (NAT 1), which is present in intestinal epithelial cells and liver. Adverse effects of mesalamine compared with salazopyrine was in the placebo range. It is found that, Local concentrations in the colonic and small bowel mucosa is a determinant the clinical outcome in IBD. Much awaited modified drug delivery systems were designed to release sufficient drug

to sites of inflammation were approved and is in use. Mesalamine also is being tried in Diverticular disease, chemoprevention of colorectal cancer etc.



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