



CHRONOGRAPHY OF INFLAMMATORY BOWEL DISEASE

Year 1977: The active component of sulphasalazine is 5-aminosalicylic acid[☆]



Año 1977: el componente activo de la sulfasalazina es el ácido 5-aminosalicílico

Fernando Gomollón^{a,b,c,*}, Ignacio Marín-Jiménez^d

^a Unidad de Enfermedad Inflamatoria Intestinal, Servicio de Aparato Digestivo, Hospital Clínico Universitario Lozano Blesa, Instituto de Investigación Sanitaria Aragón (IIS Aragón), Zaragoza, Spain

^b Centro de Investigación Biomédica en Red en el Área temática de Enfermedades Hepáticas (CIBEREHD), Madrid, Spain

^c Departamento de Medicina, Universidad de Zaragoza, Zaragoza, Spain

^d Unidad de Enfermedad Inflamatoria Intestinal, Servicio de Aparato Digestivo, Hospital Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón (IISGM), Madrid, Spain

In 1941, Nana Schwartz had introduced salazopyrin combined with an antibiotic (a sulfamide) with a presumed analgesic (5-aminosalicylic acid) to control as far as possible the, presumed infectious, rheumatoid arthritis of the King of Sweden. She got it right with an immunomodulating molecule that we still use. Some patients with chronic diarrhoea improved, and it began to be used in ulcerative colitis, with the Truelove group being that which contributed the most to finding evidence of its usefulness in ulcerative colitis. But, what really was the *active* component? This

is not a trivial question, since salazopyrin was associated with significant adverse events on occasion or if the dose was high. This study is a wonder of ingenuity: patients with colitis were treated with salazopyrin, sulfapyridine or mesalazine: mesalazine enemas were equally effective as the mother molecule, while sulfapyridine alone was clearly inferior. This idea led to the development of mesalazines that we use today, and that are the basis of treatment for most patients with ulcerative colitis, with one of the safest drugs that we use in digestive medicine.

[☆] Please cite this article as: Gomollón F, Marín-Jiménez I. Año 1977: el componente activo de la sulfasalazina es el ácido 5-aminosalicílico. Gastroenterol Hepatol. 2020;43:369–370.

* Corresponding author.

E-mail address: fgomollon@gmail.com (F. Gomollón).

An experiment to determine the active therapeutic moiety of sulphasalazine

Azad Khan AK, Piris J, Truelove SC. Lancet 1977;2(8044):892-5

1977: The active component of sulfasalazine is 5-aminosalicylic acid



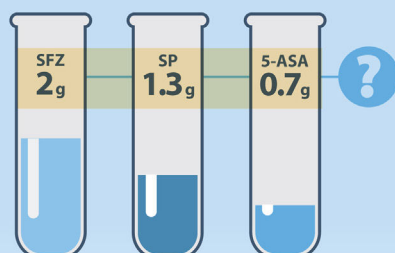
SFZ works in UC but...

...is it due to one of its components (SP and 5-ASA) or both?



Determining the active component of sulfasalazine

Randomized, double-blind, controlled therapeutic trial in which retention enemas were administered of each of the three components.



Effects on inflamed mucosa

Abbreviations:

5-ASA: 5-aminosalicylic acid; UC: ulcerative colitis; SFZ: sulfasalazine; SP: sulfapyridine.



Patients

Inclusion criteria



- ✓ Mild or moderate UC.
- ✓ In clinical remission, but sigmoidoscopic inflammation.
- ✗ Oral or rectal corticosteroids or azathioprine.



Method

- First flare
- Relapse
- Remission, but with inflammation

SFZ

N = 22



5-ASA

N = 21



SP

N = 19



Results

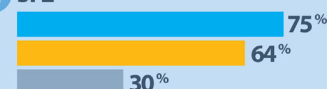
Objectivity

Clinical and histological response

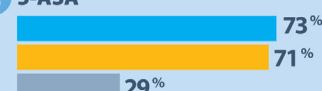
Percentages of improvement based on the enema

■ Clinical ■ Endoscopic ■ Histological

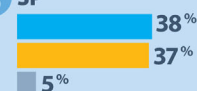
SFZ



5-ASA



SP



Conclusions

- 1 SFZ and 5-ASA share a common therapeutic activity, absent in SP.
5-ASA = active component
SP = transporter
- 2 SFZ and 5-ASA inhibit the synthesis of prostaglandins, which are involved in inflammation and are common in greater numbers with active UC.
- 3 Possibility of synthesising new drugs with the therapeutic activity of SFZ but without the majority of its side effects.