

Sodium and Acid Saccharin Purity

Some time ago we started a project that had as first objective to improve the quality of our saccharin. We developed a new industrial process and now we are producing saccharin by this new process.

Our actual process provides us with the best quality. This advance permits us to change our Technical Specifications for the saccharin and to restrict more all the impurities present in the saccharin than the pharmacopoeias. The most important differences between our new Technical Specifications and the maximums shown in the European and 95/31/EC are resumed as follow:

	P. ADITIVOS SPECIFICATIONS	EUROPEAN PHARMACOPOEIA	EC 95/31/EC
<i>Impurities</i>			
<i>p-Toluensulphonamide</i>	<3 ppm	<10 ppm	<10 ppm
<i>o-Toluensulphonamide</i>	<3 ppm	<10 ppm	<10 ppm
<i>1,2-benzisotiazoline-3-one (BIT)</i>	<5 ppm	No limited	No limited
<i>Methyl anthranilate</i>	<1 ppm	No limited	No limited
<i>p-sulphonamidobenzoic acid</i>	< 10 ppm	No limited	<25 ppm
<i>Residual solvents</i>			
<i>Toluene</i>	< 1 ppm	< 900 ppm	No limited
<i>Methanol</i>	< 5 ppm	< 3000 ppm	No limited
<i>Microbiology</i>			
<i>Total aerobic bacteria</i>	< 100 cfu/g	No limited	No limited
<i>Total coliform bacteria</i>	Absence/0.1 g	No limited	No limited
<i>Salmonella spp</i>	Absence/25 g	No limited	No Limited

We can offer our customers a high quality saccharin. Our Technical Specifications are more restrictive than the maximums of the European Pharmacopoeia or European Directive. We introduce more parameters and new restrictions for the impurities.

The analyses of these impurities are based on the Gas Chromatographic methods described in the European Pharmacopoeia, 4th Edition.

Fig. 1 and *Fig. 2* show the gas chromatography of two samples of our Sodium Saccharin (lot number 65/02) and Acid Saccharin (lot number 48/02). *Fig 3* shows the reference extraction analysis. The internal patron is caffeine (retention time 5.3 minutes) and picks with retention time 0-1.5 minutes correspond to the solvent used in the extraction.

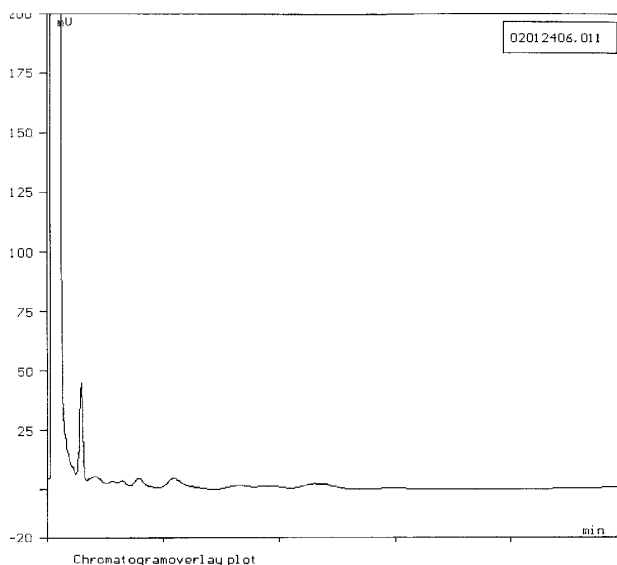


Fig. 1.- Sodium saccharin
PRODUCTOS ADITIVOS.
Lot number 0065/02
European Pharmacopoeia analysis conditions

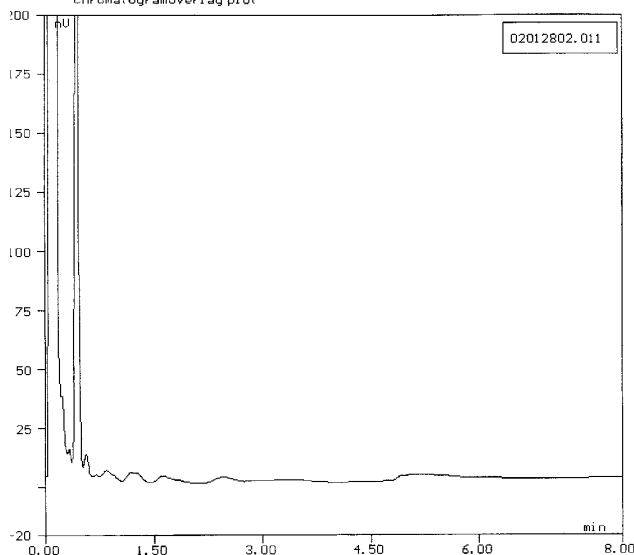


Fig. 2.- Acid saccharin
PRODUCTOS ADITIVOS.
Lot number 0048/02
European Pharmacopoeia analysis conditions

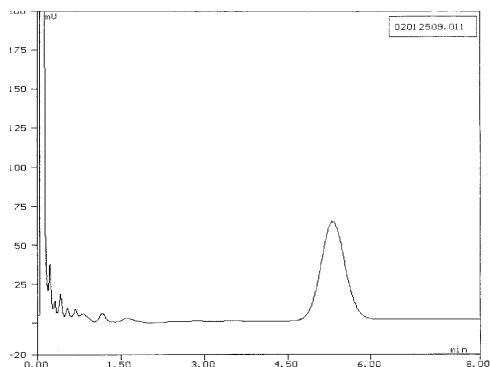


Fig. 3.- Reference extraction analysis
Retention time at 5.3 minutes correspond to the internal patron (caffeine)
Picks at retention time 0-1.5 minutes correspond to the solvent extract
European Pharmacopoeia analysis conditions.

In Fig. 1-2 we don't use the internal patron because we detected in most part of the commercial saccharin unknown impurities at the same retention times.

Our new purification process is based on different chemical and physical steps. Now we are able to convert most important impurities in saccharin and to get saccharin free of impurities (Fig. 1-2)

Apart from the development of this knew industrial process we started the analysis of the most important saccharins presents in the European market. *Fig-4* and *Fig-5* are two representative examples of it. In all these saccharins there are a high percentage of unknown impurities and they don't correspond to the *o*- and *p*-toluensulphonamide. They are not described at the pharmacopoeia and in some cases these impurities are present in percentages up to 400 ppm.

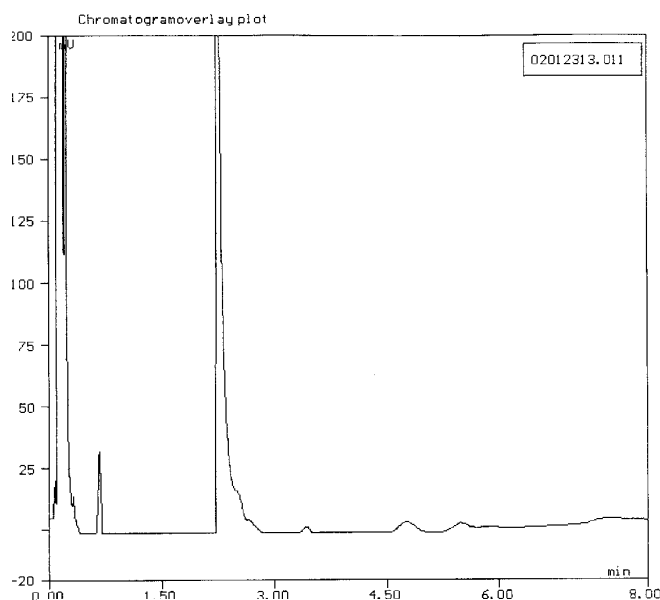


Fig. 4.- Commercial saccharin-1
European Pharmacopoeia analysis conditions.

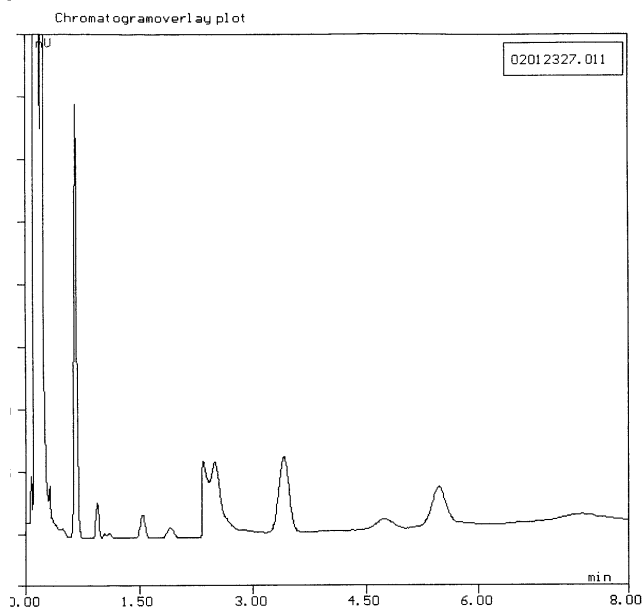


Fig. 5.- Commercial saccharin-2
European Pharmacopoeia analysis conditions.

All these products don't comply with the Pharmacopoeia: they present non-identified impurities (others than o- and p-toluensulphonamide) and their percentages are higher than 10 ppm (maximum levels for the o- and p-TS).

We analysed these non-identified impurities by mass spectroscopy in order to know their identity.

CONCLUSIONS

- Our saccharin has a very high quality.
- Our new industrial process permits us to offer to our customers saccharin free of impurities.
- Our Technical Specifications are more restrictive than the European Pharmacopoeia and European Directive.
- We introduce new restrictions on some important not identified impurities.
- We analysed commercial saccharins. In the majority of the cases they have non-identified impurities and their percentage is higher than 10 ppm (maximum specified in the Pharmacopoeia or European Laws for o- and p-Toluensulfonamide).