Natural organo-sulfur compounds inhibit RBL-2H3 mast cell degranulation

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Hydrogen sulfide (H_2S) is an endogenous gasotransmitter involved in the regulation of many physiological mechanisms in the cardiovascular, respiratory, gastroenteric, endocrine and central nervous systems. Moreover, H_2S is deeply involved in regulatory inflammation, although there is no clear consensus as to its precise role in inflammatory signalling (Whiteman et al., 2011).

In the last years there has been an increasing interest in natural drugs. In particular, erbal exogenous compounds, which exhibit the pharmacodynamic profile of H_2S, are viewed as useful tools for promising pharmacotherapeutic agents.

On these bases, it would be appropriate to investigate the influence of H_2S, released from synthetic and natural compounds, on mast cells (MC), which are widely recognized as players in inflammatory and allergic reactions.

In this regard, derivatives of Alliaceae, a botanical family rich of organo-sulfur compounds, have been widely investigated regarding their therapeutic applications. Moreover, it has been proven that the sulfur compounds of garlic such as diallyl disulfide (DADS) act as slow H_2S-releasing compound, requiring the presence of reduced glutathione (Benavides et al., 2007).

Beyond these natural organic polysulfides, another class of compounds is emerging. Cruciferae vegetables including broccoli, cabbage, watercress, and cauli?ower are reported to play protective roles in different diseases. The anti-in?ammatory effect of cruciferae vegetables is attributed to organic isothiocyanates (ITCs) (Stoewsand, 1995). The high contents of ITCs have been implicated as being responsible for the biological effects of these vegetables.

In order to evaluate the potential anti-inflammatory effects of natural and synthetic sulfur-containing molecules, in this experimental work the MC-like RBL-2H3 cell line (Rat Basophilic Leukemia) was used. The degranulation process was pharmacologically induced by antigenic stimulus (monoclonal anti-dinitrophenyl antibody (DNP)) and non-antigenic stimulus (Ionomycin and Thapsigargin). The release of β-hexosaminidase has been measured as a reliable marker of MC degranulation by means of spectrophotometric assays.

NaHS, a fast H_2S-donor used as reference drug, inhibited in a concentration-dependent manner the DNP-induced MC activation. By contrast, NaHS did not inhibit the MC activation due to Thapsigargin and Ionomycin, suggesting that its inhibitory mechanism is strictly linked to the interaction with FcεRI receptor or FcεRI-associated signalling. IS-176, a synthetic benzothioamide behaving as a slow H_2S-donor, turned out to be able to inhibit MC degranulation with a concentration-dependent manner comparable to NaHS. As concerns natural compounds, different glucosinolates and ITCs belonging to the Brassicaceae family, such as sinigrin, allyl-ITC (AITC) and phenyl-ITC (PhITC), were tested. They all showed an inhibition of MC degranulation with different results. In particular, AITC and PhITC fully abolished the β-hexosaminidase release with a clear concentration-dependent manner.

The strong inhibition of MC degranulation by these natural organo-sulphur compounds is greatly promising. Therefore, future studies will aim to explore the effects of further organo-sulfur compounds and investigate their mechanism of action.

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Stoewsand (1995) Food Chem. Toxicol. 33(6):537-43.
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