Non-antigenicity of a salicylamide derivative of aspirin

Weiner, Rosenblatt & Howes (1963) have shown circulating antibodies against aspirin in sera of patients allergic to aspirin and rabbits immunized with aspirin-protein conjugates, using the tanned red cell agglutination technique. One remarkable feature of aspirin hypersensitivity is that individuals who react to aspirin rarely do so to salicylates. It has been shown (Schwartz & Amidon, 1966) that aspirin can react with amines to produce a salicylamide derivative whereas salicylic acid does not, though a very small proportion of the original aspirin reacts with amines to produce the salicylamide derivative. Schwartz & Amidon (1966) considered that if salicylamide derivatives could be proved to be the antigenic determinant in hypersensitivity to aspirin, it might offer a possible explanation for the lack of hypersensitivity to salicylates by patients known to be allergic to aspirin. We now report that the salicylamide derivative of aspirin does not act as an antigen.

N-Salicyloylglycine was prepared by refluxing glycine (0·03 mol) with sodium hydroxide (0·08 mol) and phenyl salicylate (0·02 mol) for 4 h, the mixture was cooled, acidified and precipitates crystallized from chloroform–methyl acetate (3:1).

The test solution of *N*-salicyloylglycine was prepared in sterile isotonic saline solution in a concentration of 1% amino-acid. Two groups of rabbits, each animal being more than 2·5 kg were treated. One was immunized with the test solution and the other with the test solution blended with an equal volume of complete Freunds' adjuvant (Feinberg & Malkiel, 1951). The animals were bled periodically for the detection of antibodies.

The indirect haemagglutination test using tanned sheep red blood cells (Stavitsky, 1954) and gel precipitation techniques were used for detection of circulating antibodies against *N*-salicyloylglycine in the sera. A group of guinea-pigs was passively sensitized by intraperitoneal injection of 5 ml of immunized rabbit serum and challenged after 48 h by intravenous injection of the derivative. Another group of guinea-pigs was actively immunized and challenged after 2 weeks (Feinberg & Malkiel, 1951).

No circulating antibodies were demonstrable in the sera of immunized rabbits. Guinea-pigs immunized either passively or actively did not show sign of anaphylaxis when challenged.

Hence, it seems that the salicylamide derivative is not antigenic by itself. Different authors (Weiner, Rosenblatt & Howes, 1963; Wicher, Schwartz & others, 1968) have shown that when rabbits were immunized with aspiryl conjugates of high molecular weight proteins like crystalline egg albumin or bovine γ-globulin, circulating antibodies could be demonstrated in the immune sera to very high titres. It seems most probable that a complex protein molecule may be responsible for imparting antigenicity to aspirin-protein conjugates rather than a simple amine which reacts with aspirin to give salicylamide derivatives.

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