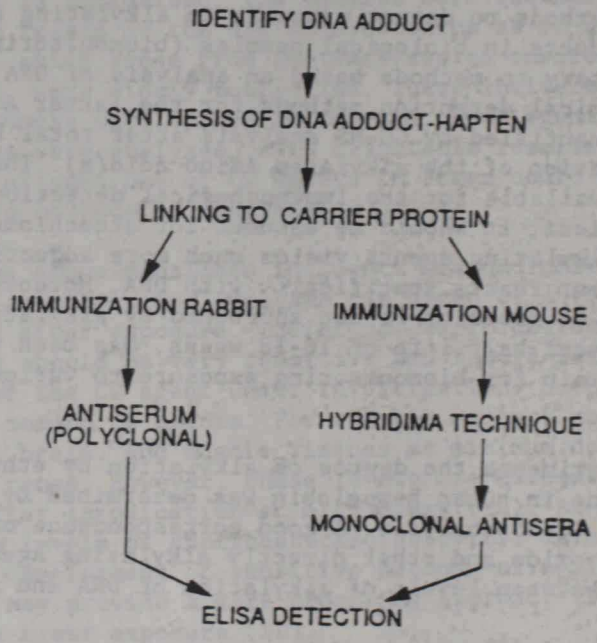
2. APPROACH

Before dealing with the work on sulfur mustard, it may be useful to summarize how an immunochemical detection method against adducts of small molecules like sulfur mustard is developed (see Scheme 1). The reaction of alkylating agents with DNA or proteins generally results in a number of different types of adducts, because of reaction with various components of the macromolecule. Therefore, before antibodies to one of these adducts can be raised, its chemical structure should be established. Next, a relatively small molecule is synthesized that comprises all essential structural elements of the adduct. This "hapten" is usually not suitable for direct use in immunizations, because it is too small to elicit an immune response. Therefore, the hapten is synthesized in such a way that it contains a "handle" which serves to couple it to a carrier protein. The protein, carrying multiple hapten molecules, is used for immunization. It is injected into rabbits in order to raise polyclonal antibodies against the adduct.



Scheme 1 Approach for the development of an immunochemical detection method for adducts to DNA.

This gives an antiserum having various antibodies in it, with a range of affinities for the adduct. It can be used to develop quickly the immunochemical detection techniques before monoclonal antibodies with a homogeneous affinity for the adduct have been raised, which is a rather time consuming effort. In order to obtain monoclonal antibodies, mice are immunized. Then, spleen cells are fused with immortal plasmacytoma cells. The fused cells, i.e., the so-called hybridomas, are selectively cultured in a special medium. Next, they are selected on the basis of the production of adduct-specific antibodies. Subsequently, they are diluted until single clones are obtained. Each of these