test makes the assignment of clear reaction pathways impossible. However, a number of suggestions can be made concerning the mode of formation of some of the products.

(i) Benzenesulphonamide, but not benzoic acid, is formed indicating that decarbonylation of saccharin (or decarboxylation of a derivative of it) takes place.

(ii) Benzonitrile may be formed either by dehydration of the imide group, or by attack of some aromatic species by CN^- formed *in situ*. The former is favoured since no CN^- was detected in the residue, and both benzamide and nicotinamide were converted into their nitriles by soda lime pyrolysis.

(iii) It is possible that aniline is formed through attack by NH_2^- on an aryne intermediate (i.e. by elimination-addition) but more probable that direct nucleophilic displacement of a sulphonate (or related) group occurs. Jackson & Wing (1886) have shown that the fusion of sodium amide with salts of aromatic sulphonic acids produces primary aromatic amines in low yield.

(iv) Carbazole is probably formed from aniline via the intermediate diphenylamine, since Braun & Grieff (1872) showed that distillation of either of these with lime gave carbazole.

(v) Under the reductive conditions of the test it is likely that benzene-sulphonamide is deaminated and converted into thiophenol, which may dimerize to form diphenyl disulphide. The latter would readily decompose on heating to diphenyl sulphide in a manner similar to that described by Heldt (1965) for *p*-tolyl disulphide.

(vi) The formation of benzene and biphenyl can be accounted for by assuming that phenyl radicals or ions are liberated which either combine with hydrogen or couple together. Reasonably good yields of *p*-bitolyl were obtained by Heldt (1965) from *p*-tolyl sulphide upon pyrolysis over metal oxide catalysts.

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Effect of sodium carboxymethylcellulose and compound tragacanth powder on the sedimentation and redispersal of sulphadimidine mixture, paediatric B.P.C. 1968

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This communication is a report on the physical stability of Sulphadimidine Mixture, Paediatric B.P.C. 1968, when prepared with sodium carboxymethylcellulose 50 or, extemporaneously, with compound tragacanth powder. Previous studies on the evaluation of factors controlling the physical stability of sulphonamide suspensions were conducted mainly on model systems (Haines & Martin, 1961; Wilson & Ecanow, 1963; Ecanow, Grundman & Wilson, 1966; Jones, Matthews & Rhodes, 1970).

Sulphadimidine Mixture, Paediatric B.P.C. 1968 was prepared using 1% sodium carboxymethylcellulose 50 or 4% compound tragacanth powder, as described in the British Pharmaceutical Codex (1968). Care was taken to minimize air entrainment into mixtures. Sedimentation heights were recorded as suggested by Martin (1961). Samples for particle size analysis were withdrawn at a fixed depth at the midpoint of settling mixtures, diluted 1:50 with filtered 1% sodium chloride solution and assayed using a Coulter Counter "Model B" Industrial, fitted with a 400 μm orifice tube (Coulter Electronics Limited, Dunstable). Redispersibility was measured as described by Matthews & Rhodes (1968). Mixtures were stored for periods up to 21 days in a constant temperature room at $20° \pm 1°$.

The initial sedimentation rate of the mixture containing 4% compound tragacanth powder was more rapid than for the mixture containing 1% sodium carboxymethylcellulose 50. However, as the period of storage was extended beyond 8 h the reverse effect occurred. Falling sphere viscosity measurements indicated that during this storage period constituents of the compound tragacanth powder settled, gradually forming a viscous sol. The latter initially produced a viscosity gradient in the mixture which increased progressively with depth. These findings would contribute to an explanation of the observed sedimentation rates. Size

analysis of particles over 40 μm showed that at equivalent times the diameter corresponding to a cumulative % oversize (volume), except 100%, was greater for the compound tragacanth mixtures. Photomicrographs taken at these times showed evidence of sulphadimidine—compound tragacanth aggregates sedimenting, which would account for the difference in size distributions obtained. At equivalent sampling times, the mixture containing the compound tragacanth powder was increasingly more difficult to redisperse to homogeneity than the mixture containing sodium carboxymethylcellulose 50.

The rapid appearance of a large supernatant layer and the caking tendencies of both suspensions during storage are undesirable. Studies are in progress on the use of agents to aid the optimum formulation of sulphadimidine suspension.

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A possible mechanism for the action of dimethyl sulphoxide on percutaneous absorption

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In vitro experiments have been carried out to assess the effect of DMSO on the physicochemical properties of hyaluronic acid and chondroitin sulphate in aqueous solution. Hyaluronic acid and chondroitin sulphate are both present in skin. Day (1952) and others (Laurent & Petruszkiewicz, 1961) have shown that the former plays an important part in the resistance of flow through connective tissue. It exists in solution as a meshwork of long molecules which can impede the passage of even small molecules through the solution. It is therefore feasible that hyaluronic acid plays a part in resisting the percutaneous transport of large and small drug molecules.

A three-compartment cell was used. The aqueous solution of sodium hyaluronate or chondroitin sulphate was placed in the central compartment between two membranes separating the donor and recipient compartments. The rate of diffusion of the methylene blue and salicylic acid into the recipient cell was noted in the presence and absence of DMSO (see Table).

Table 1. *Rates of diffusion on methylene blue and salicylic acid through hyaluronic acid*[1] *and chondroitin sulphate*[2] *gels.*

Solvent	Methylene Blue - hyaluronic acid* (1 mg ml^{-1})	10^4K (g cm^{-2} min^{-1}) Methylene Blue - chondroitin sulphate (20 mg ml^{-1})	Salicylic acid - hyaluronic acid* (1 mg ml^{-1})
Water or buffer	2	4	7·3
10% DMSO	4	5·6	15·0

* Molecular weight, from viscosity measurements, $8{\cdot}9 \times 10^5$.

[1] Sigma grade III P. [2] Sigma grade II mixed isomers.

10% DMSO reduces the intrinsic viscosity of hyaluronic acid solutions from 1550 to 900 ml g^{-1}, which implies a reduction in the axial ratio of the hyaluronic acid from 156 to 120.

The experimental data support the view that DMSO exerts its absorption-enhancing effects by decreasing the microscopic viscosity of the barrier layers, thereby decreasing the resistance offered to diffusing solute molecules.

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