

need for research on the synergetic or antagonistic action, as the case may be, of one vitamin on another. More information is obviously needed to put the practice of combining more than one vitamin in a single preparation on a sound theoretical basis.

LT.-COL. SOKHEY, who presided over these deliberations, correctly pointed out how manufactures in the country had not availed themselves of the opportunities afforded by the war and had resorted to mere compounding, mostly out of imported pharmaceuticals. Doubtless, there are difficulties in the way of the development of a synthetic drug industry in the country, chief among them being, as mentioned by Dr. R. D. Desai, the need for dependence on foreign imports for a variety of intermediates which cannot be manufactured in the country until the heavy chemical and coal-tar industries get securely established. In this connection, an aspect of drug production that came for little discussion related to bio-synthesis from agricultural and industrial waste products. A host of substances of therapeutic value, like lactic, citric and gluconic acids, food yeast and antibiotic mould metabolites could well be prepared by fermentation processes without dependence upon imported intermediates.

There was unanimity underlying the discussions on the second symposium on the future of pharmacy in the country. The speakers stressed on the need for (1) control of pharmaceutical practice by limiting it to a properly qualified group of people as in most parts of the world, and (2) a uniform central legislation for drugs and pharmacy combined. In opening the discussion, DR. B. MUKERJI referred to the present deplorable position of the profession of pharmacy in India and emphasized how there can be no practice of pharmacy without the aid of medicine and how both the professions should, therefore, work hand in hand and strive together to achieve the goal of a higher standard of national health and fitness.

DR. R. R. NANJI gave a brief review of the growth and development of pharmaceutical education in England and other countries abroad and showed how India was probably a century behind most civilised countries in this respect. He also outlined certain legislative measures aiming at improvements in the standard of training and qualifications of pharmacists and suggested the creation of a Central Pharmacy Board for the general control of the profession.

The Central Government have recently enacted a Drug Act, 1940, and are shortly proposing to enact Drug Rules under this Act, which take cognisance of the urgent needs of the country outlined above. These are happy auguries, for, statutory control over what is at present only a chaotic situation is bound to raise the status and prestige of Indian Pharmacy and bring in its wake a better economic position for the pharmacist and a lasting recognition as an active partner of the noble public health profession. A detailed account of the proceedings of the Conference will appear as a Special Number of the *Indian Journal of Pharmacy*.
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SUBSTANTIVITY OF DYES IN RELATION TO CHEMICAL CONSTITUTION*

SUBSTANTIVITY is not an absolute property and it is difficult to define. There is no sharp demarcation between substantive and unsubstantive dyes. All direct dyes tend to form colloidal solutions. Particles in molecular solution diffuse through the fibre and do not function in the dyeing process, unless there is a change in their state of aggregation due to an alteration in conditions.

There are a few natural colouring matters (bixin, carthamin, curcumin), which are substantive to cotton, and which do not contain nitrogen or sulphur; but the synthetic direct cotton colours are the sodium salts of aromatic sulphonic acids containing nitrogenous groups. Cotton takes up these dyes in the form of neutral sulphonates. Further, marked substantivity to cotton is shown by the leuco compounds of sulphur dyes and of the anthraquinonoid vat dyes, including those not containing nitrogen and sulphur, and the aryl-amides of hydroxynaphthoic acid.

The structural features favourable to substantivity in azo dyes are now well recognised. Following Schirm's hypothesis of conjugated unsaturation, Hodgson has postulated a coplanar configuration of the aromatic nuclei as a necessary condition for the production of substantivity. Coplanarity in a dye molecule is an advantage for attachment to the cellulose chain, but there are at least two recorded instances of non-coplanar dyes with substantivity for cotton. Sen and Sadasivam noticed that the dye from tetrazotised 2:2'-di-hydroxy-methyl-benzidine and β -naphthol-6-sulphonic acid was substantive. The significant factor here is probably the hydroxyl in each of the groups in the 2:2'-positions; the hydroxyls could anchor themselves by hydrogen bonding to the glycosidic oxygens in suitably situated chains of the cellulose macro-molecule, so that a complicated, but easily conceivable, molecular network between dye and cellulose develops. The second example is a new class of substantive azo dyes described by Allen and Pingert (1944), which are derived from 4:4'-diamino-*o*-terphenyl and which cannot be coplanar.

Among similar groups of dyes, the substantivity increases from the benzene to the naphthalene, anthracene and the more complex, condensed polynuclear aromatic hydrocarbon series. This is not due to the mere increase in molecular weight, but the special characteristics of the valence-bond structures are involved. The leuco compounds of the anthraquinonoid vat colours as a class are characterised by high substantivity. The leuco compounds, for instance, of dibenzanthrone, its 16:17-dimethoxy derivative and isodibenzanthrone are very highly substantive; and the complete absence of nitrogen and sulphur, invariable constituents of the direct cotton colours, will be noticed. The alkaline solutions of the reduc-

* Abstract of Dr. K. Venkatraman's Presidential Address to the Section of Chemistry, Indian Science Congress, Nagpur, 1945.

tion products (or 'vats') of some of the anthraquinone vat dyes have such high affinity for cotton, and the baths are so rapidly exhausted, that the dyeing process has to be retarded and controlled by the addition of restraining and level dyeing agents, consisting of glue or synthetic protective colloids.

The substantivity of the anthraquinonoid vats is associated with the resonance among numerous valence-bond structures by which the higher condensed ring systems can be represented. The angular ring systems have a larger number of stable resonating structures and a larger resonance energy than the corresponding linear ring systems. Angular configuration of condensed ring systems is a common feature of anthraquinone vat dyes. Among the isomeric dihydro-anthraquinone-azines, the commercial product which possesses the substantivity necessary for practical dyeing is indanthrone, having the bis-angular orientation. Other examples are the bis-acridone, Indanthrene Violet BN and the tetracarbazole, Indanthrene Khaki GG. The more complex the polynuclear system and the greater the number of benzene rings, the larger will be the resonance energy. One effect of resonance will be coplanar configuration of the molecules. It would appear that there is a broad correlation between the number of stable resonance forms and the resonance energy on the one hand, and the substantivity on the other, of the leuco compounds of anthraquinone vat dyes.

The older conceptions of substantive dyes as those possessing long thread-like molecules of approximately straight line form, which were based on the benzidine type of azo dyes, must be modified in view of the constitution of the highly substantive leuco compounds of the anthraquinone vat dyes. The affinity of a complex polynuclear dye such as Indanthrene Khaki GG probably involves the attachment of the dye molecules to several parallel cellulose units at suitable points, so that the dye molecules act as bridges or grids in a three-dimensional network.

While the indigoid and thioindigoid vats are yellow, the anthraquinone vat dyes give intensely coloured vats; Indanthrene Yellow G thus gives a deep blue vat. Alkaline reduction of an anthraquinone vat dye produces auxochromic hydroxyl groups which introduce much greater possibilities of resonance than in the case of leuco-indigoids, on account of the large number of aromatic ring systems. Bathochromic effect and substantivity do not always go together, but there seems to be enough evidence to believe that the resonance factors favourable for intense colour are also favourable for substantivity in the anthraquinone vats, the requirements regarding the degree of dispersity in aqueous solution being satisfied.

The conversion of the leuco-forms of vat dyes to the sulphuric esters, the sodium salts of which are marketed as Indigosols and Soledons, greatly reduces the substantivity. The Soledon has a much lower substantivity than the alkaline vat. The reduction in substantivity may be correlated with the change in the colloidal and electrochemical character of the solution, as well as the restraining influence of the sulphonic group on the resonance of the molecule. Among the Indigosols and Soledons, the anthraquinone derivatives have in general higher substantivity than the indigo and thioindigo derivatives, and in the former group

the substantivities run roughly parallel with those of the vats of the parent-dyes.

Schirm has attributed the substantivity of Naphtol AS to conjugation due to enolisation of the -CONH- group, but the constitutional factor fundamental to the substantivity of the naphthols is the hydroxyl adjacent to the -CONH- group, and this must play a part in the attachment to cellulose. Among the facts to be borne in mind in considering the structural forms of the "naphthols" are the substantivity in alkaline solution with consequent ionisation and the speed with which the "naphthols" couple even with very weakly polarised diazo salts, indicating the anionoid character of the *l*-carbon atom. Several valence-bond structures may then be suggested as the predominating resonance forms. The essentiality of the 2-hydroxy-3-carboxamide grouping and the nonsubstantivity of the isomers are probably concerned with steric factors governing the attachment of the reactive centres in the naphthol to the cellulose chain. Such steric factors are apparently also involved in the greater substantivity of the β -naphthylamide of hydroxynaphthoic acid in comparison with the α -isomer. The increase in substantivity by replacing the naphthalene nucleus in the acid half or the benzene nucleus in the amine half of the Naphtol AS molecule by more complex and condensed ring systems is related to the resonance among more numerous valence-bond structures and the larger resonance energy.

The constitutional factors which are favourable to the substantivity of dyes towards cellulose are summarised as (a) conjugated unsaturation; (b) coplanarity of the ring systems; (c) condensed ring systems, representing a large number of resonating forms and high resonance energy; (d) heterocyclic nuclei; (e) specific atoms and groups in suitable positions; (f) dipole characteristics; polar groups of opposite character connected by a conjugated system, leading to a large amplitude of resonance and a large polarisability; (g) colloidal character in aqueous solution, and a balance between the hydrophobic and hydrophilic parts of the molecule.

Measurement of interatomic distances between the reactive centres in dye molecules in their stable resonance forms, and their relation to the interatomic distances between the reactive centres in the cellulose chain, might ultimately give us a picture of the mode of attachment of dyes to cellulose. Since the cellulose macromolecule contains a very large number of both electron-donor oxygen atoms and electron-acceptor hydroxylic hydrogens, the affinity of cellulose for dyes with high molecular resonance structures, having a large amplitude of resonance and a large polarisability, is not difficult to visualise in general terms. Hydrogen bonding readily suggests itself as the likely mechanism of the intermolecular dye-cellulose attachment in view of the strength of the linkage and the rapidity of dyeing processes. However, there is a long way yet to go before complete theories of the colour of dyes and of their varying degrees of affinity for cellulose can be developed. The constitution of the whole series of substantive dyes must be studied in conjunction with the present view of the structure of cellulose as a network of discrete, crystalline micelles together with amorphous regions of disorderly orientation.