

tion was detectable when the concentration of noradrenaline was as low as 2×10^{-7} ml⁻¹.

In cardiac tissue Ehinger, Falck & Sporrang (1970) found adrenergic terminals in close apposition to cholinergic terminals. Thus in rat atrium, taken from an animal treated with 5-hydroxydopamine 4 h previously, they found profiles in contact, one with vesicles with dense cores which were adrenergic, and the other with agranular vesicles which were cholinergic. Presumably the noradrenaline was released from the adrenergic profile by acetylcholine in a layer surrounding the profile as Eränkö, Rechartd & others (1970) found in their pineal results, and not by the acetylcholine released from the cholinergic profile. This might release acetylcholine to act as an inhibitory mechanism of the kind suggested by Muscholl. But where sympathetic and parasympathetic fibres are not intermingled, there seems to be no evidence of "muscarinic" inhibitory receptors.

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The calculation of the tensile strength of tablets

Recently, Rowe, Elworthy & Ganderton (1973), in a calculation of the tensile strength of compacts from the diametral compression test, suggested that an allowance is necessary to enable a comparison of compacts of different porosities to be made. However, the validity of the allowance they propose would seem open to question.

The maximum tensile stress in a cylinder of elastic material loaded in compression along a diameter is given by the equation (Frocht, 1948) where P is the applied

$$\sigma_t = \frac{2P}{\pi Dt}$$

diametral load, D is the diameter of the cylinder and t is its thickness. This maximum stress is approximately constant over almost the entire length of the loaded diameter.

At failure the value of the maximum tensile stress σ_t represents the tensile strength of the sample. For non-ideal materials under non-ideal test conditions, such as the testing of pharmaceutical tablets, the stress conditions will also not be ideal. Nevertheless, as shown by Peltier (1954), for various assumed stress distributions, the tensile stress can be held uniform over a reasonable proportion of the diameter if the width of the loading area is less than 1/5 the specimen diameter. Rudnick, Hunter & Holden (1963) have pointed out that, because of the departure from ideal behaviour,

even samples which fail in tension do not have a tensile strength (calculated from the equation) which is a true value. If the test conditions are changed, then a different value for tensile strength will be obtained. (See, for example, Fell & Newton 1970; Rees, Hersey & Cole, 1970.) However, for a given set of diametral conditions, the value of the tensile strength obtained can be used for comparative purposes by application of the equation without correction. The values would be the maximum tensile strength of the specimens under the given test conditions. The inclusion by Rowe & others (1973) of a correction factor $[1/(1-\epsilon)]$, where ϵ is the porosity of the sample] is presumably intended to allow for changes in the area of contact between particles as the porosity changes. But such a correction is inappropriate, for, as pointed out by Knudsen (1959), "changes in porosity as they affect strength are only an indirect measure of changes in the critical or minimum load-bearing areas within a specimen." As pointed out by Goetzel (1950), the contact between particles is not as strong as the particles themselves. Thus the strength will depend on the area of contact at all porosities. If comparisons between bonding strengths are to be made, a correction is required for the area of contact, *not* for the porosity. As there is no means of determining the area over which contact occurs, calculation of the tensile strengths from the equation offers the best solution to the problem.

The proposed correction factor also makes no allowance for the distribution of porosity. A sample which has its porosity distributed evenly throughout will have a different breaking load from one with the same porosity concentrated in one region. Again, if the factor $1/(1-\epsilon)$ were functioning as intended, then it would really *correct* for porosity and the same tensile strength would be calculated for tablets of different porosities. Presumably this was not found. [At porosities of 0.4 the powder would be a loose-poured pile with zero tensile strength, yet $1/(1-\epsilon)$ then has a value of $1/(1-0.4) = 1/0.6 \approx 1.6$.]

The major advantage of the diametral compression test is that the tablets fail in a consistent manner, i.e. in tension, which results in greater reproducibility of breaking load (Fell & Newton, 1970). The advantage of calculating the tensile strength from the breaking load is that it converts the values to a standard form and allows comparison of samples of different dimensions (Newton, Rowley & others, 1971). While the conclusions of Rowe & others (1973) are not influenced by the method they used to calculate tensile strengths, the introduction of the $1/(1-\epsilon)$ factor is thus neither necessary nor well founded.

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