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Relationships Between the Modulus of Elasticity and Tensile Strength for Pharmaceutical Drugs and Excipients

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Abstract

The relationship between the modulus of elasticity and tensile strength for a variety of pharmaceutical drugs and excipients has been explored as a means of generating algorithms for use in computer simulations and expert systems.

From literature data two equations have been developed to enable the formulator, from knowledge of one property, to predict the other with a reasonable degree of accuracy.

Such relationships are invaluable for use in computer simulation programs or formulation expert systems, enabling formulators to screen potential formulations quickly without the need for extensive experimental work.

A knowledge of the mechanical properties (specifically the modulus of elasticity, yield stress, tensile strength and critical stress intensity factor) of both drugs and excipients is important in the identification of both their compaction behaviour/ability to form compacts (Roberts & Rowe 1987; Rowe & Roberts 1995a) and their comminution behaviour (Roberts & Rowe 1999). The data are also necessary for both computer simulation programs to investigate crack propagation (Rowe & Roberts 1993, 1994) and expert systems for tablet formulation (Rowe 1993; Rowe & Roberts 1998).

Unfortunately, in many cases literature data are incomplete with many researchers reporting only one or two properties and, in these cases, it is necessary to either measure the unknown property or to use intelligent guesswork. If the cohesive energy density or solubility parameter of the material is known or can be calculated from its chemical structure it is possible to estimate the modulus of elasticity, tensile strength, critical stress intensity factor and yield behaviour (indentation hardness) using semi-empirical relationships (Roberts et al 1991, 1995a, b). If the crystal structure of the material is known the modulus of elasticity can be predicted (Payne et al 1996). We have explored the relationship between the modulus of elasticity and tensile strength for a variety of pharmaceutical drugs and excipients as a means of generating algorithms for use in computer simulations and expert systems.

All data used in the development of the algorithms have been taken from the literature where measurements and methodology are known to be self-consistent, i.e. the results are from measurements made on the same batch of material using the same methodology—either three or four point beam bending (Roberts et al 1991, 1995a; Newton et al 1993; Bin Baie et al 1996).

Figure 1 shows the relationship between the tensile strength and modulus of elasticity for thirteen materials (nine drugs, stearic acid, anhydrous lactose, α-lactose monohydrate and microcrystalline cellulose) taken from data generated by Roberts et al (1991, 1995a). If α-lactose monohydrate and microcrystalline cellulose are excluded from the analysis the equation is of the form:

$$\text{Tensile strength (MPa)} = 1.292\ \text{Modulus of elasticity (GPa)} \quad (1)$$

with a correlation coefficient r^2 of 0·9318.

It is interesting to note that the data generated by Newton et al (1993) for five benzoic acid esters all fall within the 95% confidence limits of the predicted relationship. If these data are included in the analysis the equation becomes:

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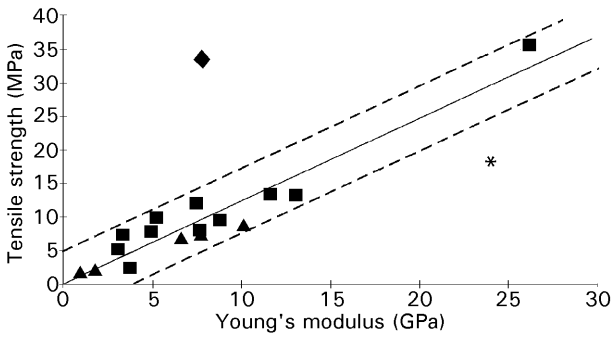

Figure 1. Tensile strength vs Young's modulus taken from the literature data: ■, data from Roberts et al (1991, 1995a); ▲ (data from Newton et al (1993); ◆, microcrystalline cellulose from Roberts et al (1991, 1995a); *, α-lactose monohydrate from Roberts et al (1991, 1995a). The straight line represents the linear regression analysis on the square data and the dashed line represents the 95% confidence limits.

$$\text{Tensile strength (MPa)} = 1.238 \text{ Modulus of elasticity (GPa)} \quad (2)$$

with a correlation coefficient r^2 of 0·9146.

The data for α-lactose monohydrate, especially the value for the tensile strength is known to be in error. This is due to the presence of cracks in the beam as has been shown by microscopy (Roberts 1991) and holographic interferometry (Silvennoinen et al 1996). It is interesting to note that recent measurements of the modulus of elasticity of α-lactose monohydrate using microindentation has confirmed the measurement by beam bending (Arteaga et al 1999).

Figure 2 shows data for a variety of cellulose derivatives, microcrystalline and powdered grades of cellulose taken from Bin Baie et al (1996), together with lines representing equation 2 and the other representing data for films of the cellulose ethers and esters (Rowe & Roberts 1995b), having a slope of 29·412. It can be seen that the data for the celluloses, although more variable, all lie between these two data sets. The apparent variability might be, in part, due to the moisture content of the beams at the time of testing since it has been shown previously that both the fracture and elasticity properties are affected by the relative humidity of the equilibrium atmosphere (Bassam et al 1990a, b). More data are needed before a representative relationship for these materials can be generated.

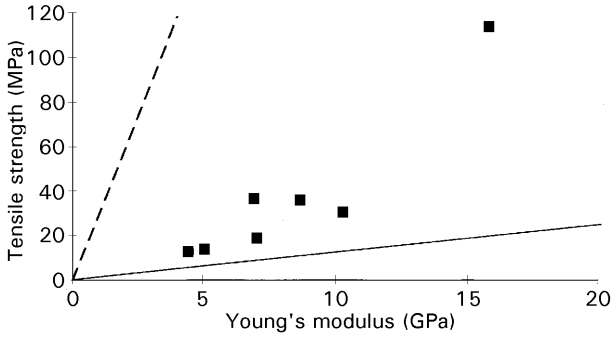

Figure 2. Tensile strength vs Young's modulus taken from literature data; ——, equation 2; – – –, data for cellulose ethers and esters from Rowe & Roberts (1995b); ■, cellulose data from Bin Baie et al (1996).

It is interesting to note that calculations of the maximum or ideal tensile strength of metals and alkaline halides give a value of 100 (Orowan 1949; Kamigaito 1988) for the slope in equations 1 and 2. However, values for single crystals and whiskers are generally lower (33 for sodium chloride, 30 for metal whiskers), similar to those calculated for cellulose ethers and esters. For organic pharmaceutical materials the value is much lower as might be expected for materials held together predominantly by Van der Waals forces and which are relatively weak when compared with metals, alkaline halides and carbon chains in polymer films. The reduction in both properties compared with the theory is due to the presence of flaws in the beams, although in each series of materials the flaw size must be consistent with the bond strength, e.g. both Young's modulus and tensile strength have been shown to be related to cohesive energy density (Roberts et al 1991, 1995a).

As can be seen, it is possible to derive empirical relationships between modulus of elasticity and tensile strength for pharmaceutical drugs and excipients. The equations developed enable the formulator, from knowledge of one property to predict the other with a reasonable degree of accuracy. Such relationships are invaluable for use in computer simulation programs or formulation expert systems, enabling formulators to screen potential formulations quickly without the need for extensive experimental work.

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