

Formulation Effect on the Mechanical Properties of Chloroquine Diphosphate Tablets

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ABSTRACT

A study has been made on the tensile strength and Brittle fracture index BFI of chloroquine diphosphate tablets at fixed parking fraction ($P_r = 0.9$) that is considered as representative of commercial chloroquine diphosphate tablets. Khaya grandifolia gum being developed as binding agent was compared with official Gelatin B.P. at variable concentrations and temperatures.

Tablets containing gelatin generally have higher tensile strength and lower BFI values than tablets containing Khaya gum. The values of tensile strength generally increased with increase in concentration of binding agent but the BFI exhibits a variable behaviour. Both tensile strength and the BFI appear to be useful indicators of the mechanical properties of chloroquine diphosphate tablets.

INTRODUCTION

The mechanical strength of a tablet provides a measure of the bonding potential of the material concerned and this information is useful to the formulator in the selection of excipients. An excessively strong bond may prevent rapid disintegration and subsequent dissolution of a drug.

The mechanical strength of a tablet can be assessed in various ways, including by fracture resistance, friability, hardness, crushing strength, transverse compression and tensile strength. Measurements of tensile strength using diametral compression are now widely employed in commercial production for controlling the strength of tablets and it is independent of tablet dimensions. The tensile strength (T) can be calculated from the equation (Fell and Newton 1970)

$$T = \frac{2F}{\pi Dh} \quad (1)$$

where F is the applied load in meganewton (MN), D is the tablet diameter in metres (m), h is the tablet thickness in metres (m).

Brittle fracture values determination is a reflection of ability of tablet formulations to laminate or cap. The brittle fracture index (BFI) was devised by Hiestand et al (1977). It is obtained by comparing the tensile strength of tablets with a hole at their center which acts as a built-in stress concentrator 'defect' with the tensile strength of tablets without a hole. The BFI is defined as

$$BFI = 0.5 \left(\frac{T_0}{T} - 1 \right) \quad (2)$$

where T is the tensile strength of the tablet without a hole

and T_0 is the apparent tensile strength of the tablet when a hole is present both at the same parking fraction. The BFI is a measure of localized stress relief within the tablet (at the edge of the hole) by plastic deformation. A low value of the BFI indicates the ability of the material to relieve localized stresses while a value approaching unity indicates a tendency of the material to laminate or cap.

In the present work, a study has been made on the comparative effect of khaya grandifolia gum, and official gelatin B.P. on the tensile strength and brittle fracture index parking fraction ($P_r = 0.9$) which is considered representative of commercial chloroquine diphosphate tablets.

MATERIALS AND METHODS

Materials

The materials used were chloroquine diphosphate (Bayer, Germany), gelatin B.P. (BPD Chemicals, Ltd, England), Khaya gum (from khaya grandifolia, Botanical garden, University of Ibadan), lactose B.P. (DMV, Veghel, Holland), corn starch B.P. (lot 70326, Pfizer Nigeria Ltd, Lagos, Nigeria)

Preparation of Granules

250g batches of the basic formulation comprising chloroquine diphosphate (65% w/w), lactose 25% w/w and corn starch (10% w/w) were dry mixed for about 3 minutes at room temperature ($\sim 25^\circ\text{C}$) in a Kenwood planetary mixer fitted with a calibrated temperature regulator. The mixture was then moistened with appropriate amounts of mucilages (Khaya gum) and solutions (gelatin) of the binding agents.

Massing was continued for about 5 minutes and the wet masses were granulated by passing them manually through a No 12 mesh (1,400mm) sieve. The granules were dried in trays in a hot air for about 24 hours at 60°C and then screened through a No 16 mesh

(1,000mm) sieve. The granules were then stored in airtight containers.

Preparation of Tablets

500mg $\pm$ 10mg tablets were prepared from the 500-1000mm size fraction of granules. The granules were poured into a 10.5mm diameter die with flat-faced and circular upper and lower punches. This was after the die and the punches had been lubricated with a 10% w/v dispersion of magnesium stearate in Acetone. The granules were then compressed in a carver hydraulic hand press (Model

C, Carver Inc. Menomonee falls, Wisconsin, U.S.A.) by the following procedure. The weighed sample was transferred into the die cavity, which was seated on the lower punch, the upper punch was fitted into place and the assembly was transferred into the hand press with subsequent lowering of the pressing head at constant rate until a predetermined pressure was attained. The pressure was maintained for 1 minute and the tablet subsequently ejected and stored in airtight container over silica gel for 24 hours to allow for elastic recovery and hardening. The tablets thus produced did not have hole in the middle.

The above procedure was repeated for the second type of tablets, but these had holes at their centre. Here the upper punch used had a hole while the lower punch was fitted with a pin the weights, W and dimensions were then determined to within 0.1mg and 0.01mm and their packing fractions P_f were calculated using equation

$$P_f = \frac{W}{V_p \cdot \rho_s} \quad (3)$$

where V_p is the volume of the tablet (including the hole when present) in CM^3 and ρ_s is the particle density of the solid material in $\text{g} \cdot \text{CM}^{-3}$

Tensile Strength Measurement

The tensile strength of tablets was determined by diametral compression using Erweka Hardness Tester (Model TDH1, Apparatebau GMBH Germany). The selector switch of the instrument was set such that the diameter (10.5mm) since 12.5 could not be obtained, it was set to 13mm. This ensured that the test jaw approached the tablet at a slow speed just prior to crushing.

The automatic operation mode was selected using the switch mode and the chosen unit of measurement of hardness was Newton (N). The tablets were fed one at a time to the middle of the test jaw. The test was started by pressing the start button. The test jaw advanced at a fast speed until it nearly touched the tablet where upon it switched to a slow speed. The pressure jaw continued to approach the tablet where upon the pressure applied was slowly increased until the tablets fractured diametrically. At the moment of breakage, the applied force was displayed on the indicator (pointer).

The motor was reversed and the pressure jaw returned at a fast speed to the starting position. After a brief pause, the pressure jaw again advanced. The short delay permitted the cleaning and hand feeding of the next tablet after the removal of the fractured one. Tensile strength was then calculated using equation (2).

Result and Discussion

The values of tensile strength (T) and brittle fracture index (BFI) for the chloroquine diphosphate tablets at packing fraction of 0.9 which was considered as representative of commercial chloroquine diphosphate tablets are presented in Table I and II for tablets containing gelatin and Khaya gum respectively, and as plots of tensile strength and BFI versus concentration of binders in figure 1 to 6 respectively. Bearing in mind the small but unavoidable differences in their moisture contents, it can be seen that an increase in the concentration of binder resulted in a systematic increase in the tensile strength of

the tablets at the chosen packing fraction. Similar results have been reported (Newitt and Conway Jones, 1958; Davis and Gloor, 1972; Escobedo and Pilpel, 1976; Kurup and Pilpel, 1979).

Generally tablets containing gelatin have higher tensile strength than those containing Khaya gum for all temperature of granules preparation. This observation may probably be due to the fact that gelatin would undergo more elastic and plastic deformation than Khaya gum under high compressive force and is therefore a stronger binding agent. This assertion is in agreement with earlier work carried out by Adeyemo (1992) on griseofulvin tablet formulations.

Through, Khaya gum at 4% w/w concentration appear to have higher tensile strength than Gelatin B.P gum at the same concentration. This may be useful information to formulators.

It was found during the determination of BFI that as expected (York and Pilpel, 1973), there was a logarithmic relationship between T or (T_0) and P_f

$$\log T \text{ or } (T_0) = AP_f + B \quad (4)$$

with a correlation coefficients > 0.98 . A and B were constants which depended on the nature and amount of binder present in the formulation and on whether the tablet had a hole in it or not. It is seen that tensile strength of a tablet with a hole was less than that of the same without a hole, the hole acting as a stress concentrator (Hiestand et al, 1977). Values of T , T_0 and BFI at P_f of 0.90 for all samples are presented in Table I and II. T was always greater than T_0 ; the values of both increased with binder concentration, while values of BFI was variable.

For the BFI parameter, tablets containing gum generally have higher BFI values than tablets containing gelatin, showing that gelatin would lower lamination tendency of tablets more than Khaya gum, and it was observed during the tableting process that some tablets containing Khaya gum had to be rejected due to visible signs of lamination. However temperature of granules preparation did not appear to have much influence on the tensile strength and BFI of the tablets.

In the present work, both T and BFI have been used to study and describe the mechanical properties of the Chloroquine diphosphate tablets studied, it would appear that these two quantities can be used to determine the mechanical properties of tablets, although the BFI appears to require more experimental investigation with various formulations to determine fully its usefulness as an indicator of the brittleness of material.

CONCLUSION

The lower values of tensile strength of Chloroquine diphosphate tablets prepared with Khaya gum as compared with the ones prepared with official Gelatin B.P. is suggestive of the fact that Khaya gum is a weaker binder. However, it may be useful in the production of antacid tablets.

The combined use of tensile strength and brittle fracture index (BFI) values appear to provide more information on the mechanical properties of Chloroquine diphosphate tablets, but some variable behaviour of the BFI suggests that further work could still be carried out to

elucidate on the determination and usefulness of the parameter.

Table I
Tensile Strength and Brittle Fracture Index (BFI)
Values for Chloroquine Diphosphate Tablets
Containing Gelatin at $P_f = 0.9$

Sample Code	Tensile Strength (MNm ⁻²)	Tensile Strength Tablets with hole (T) (MNm ⁻²)	BFI
Tablets produced from granules prepared at 25°C			
ChB	1.793	1.685	0.032
ChG 0.5	2.897	2.593	0.059
ChG 1.0	2.937	2.731	0.030
ChG 2.0	3.236	2.985	0.042
ChG 4.0	3.296	3.153	0.023
Tablets produced from granules prepared at 50°C			
ChB	1.485	1.323	0.061
ChG 0.5	1.524	1.439	0.029
ChG 1.0	1.999	1.984	0.054
ChG 2.0	2.716	2.649	0.013
ChG 4.0	3.802	2.984	0.137
Tablets produced from granules prepared at 75°C			
ChB	1.985	1.795	0.053
ChG 0.5	2.820	2.340	0.103
ChG 1.0	3.237	2.937	0.051
ChG 2.0	3.606	3.214	0.061
ChG 4.0	3.984	3.437	0.079

Sample Code Presentation

ChB = Chloroquine granules containing 0% binder
ChG 0.5 = Chloroquine granules containing 0.5% binder
ChG 1.0 = Chloroquine granules containing 1% binder
ChG 2.0 = Chloroquine granules containing 2% binder
ChG 4.0 = Chloroquine granules containing 4% binder

Table II
Tensile Strength and Brittle Fracture Index (BFI)
Values for Chloroquine Diphosphate Tablets
Containing Khaya Gum at $P_f = 0.9$

Sample Code	Tensile Strength (MNm ⁻²)	Tensile Strength Tablets with hole (T) (MNm ⁻²)	BFI
Tablets produced from granules prepared at 25°C			
ChB	1.793	1.685	0.032
ChG 0.5	2.223	1.144	0.472
ChG 1.0	2.244	1.892	0.093
ChG 2.0	2.938	1.059	0.887
ChG 4.0	7.656	3.048	0.756
Tablets produced from granules prepared at 50°C			
ChB	1.085	1.078	0.003
ChG 0.5	1.285	1.198	0.036
ChG 1.0	1.950	1.102	0.385
ChG 2.0	2.141	1.251	0.357
ChG 4.0	6.081	3.607	0.343
Tablets produced from granules prepared at 75°C			
ChB	1.085	1.078	0.003
ChG 0.5	1.644	1.311	0.127
ChG 1.0	1.726	1.275	0.177
ChG 2.0	2.218	1.935	0.073
ChG 4.0	7.603	2.775	0.880

Sample Code Presentation

ChB = Chloroquine granules containing 0% binder
ChG 0.5 = Chloroquine granules containing 0.5% Khaya
ChG 1.0 = Chloroquine granules containing 1.0% Khaya
ChG 2.0 = Chloroquine granules containing 2.0% Khaya
ChG 4.0 = Chloroquine granules containing 4.0% Khaya

Fig. 1: Tensile Strength versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 25°C at Packing Fraction = 0.9

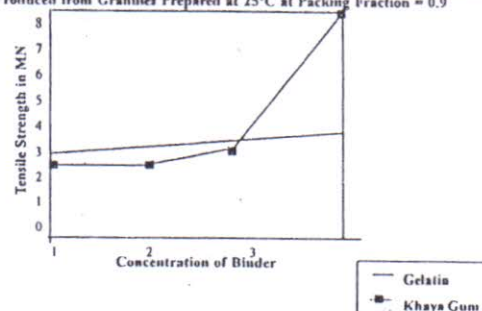


Fig. 2: Tensile Strength versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 50°C at Packing Fraction = 0.9

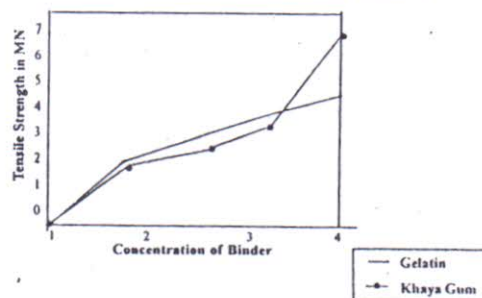


Fig. 3: Tensile Strength versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 75°C at Packing Fraction = 0.9

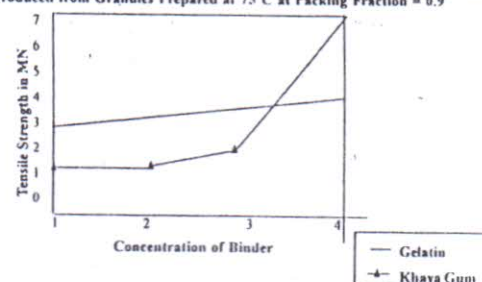


Fig. 4: Brittle Fracture Index (BFI) versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 25°C at Packing Fraction = 0.9

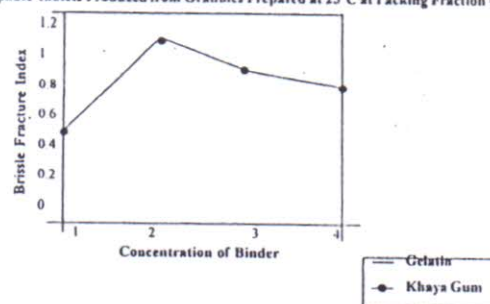


Fig. 5: Brittle Fracture Index (BFI) versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 50°C at Packing Fraction = 0.9

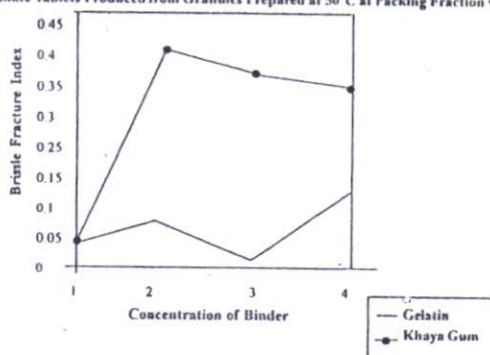
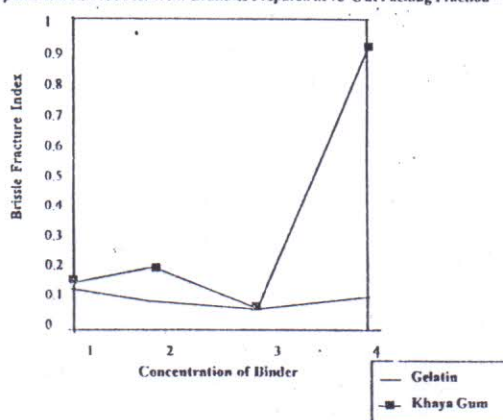


Fig. 6: Brittle Fracture Index (RFI) versus Concentration of Binder for Chloroquine Diphosphate Tablets Produced from Granules Prepared at 75°C at Packing Fraction = 0.9



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