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Evaluation of Gellan Gum as a Granulating Agent for Chloroquine Phosphate Tablets

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Abstract: Gellan gum was evaluated as a granulating agent in chloroquine phosphate tablet formulations at varying concentrations of 2.5 to 7.5% w/w. Granules were prepared using the wet granulation method. Maize starch and gelatin were employed as reference granulating agents. Prepared granules were evaluated for their micromeritic properties, while the compressed tablets were evaluated for mechanical, disintegration and dissolution properties. The effect of varying concentrations of calcium ion on the mechanical properties of the compressed tablets was also investigated. Results obtained showed that gellan gum exhibited higher binding capacity than maize starch or gelatin. The presence of calcium ions reduced the mechanical properties of the chloroquine phosphate tablets. At 0.4% w/w calcium chloride concentration, tablets with marked reduction in disintegration time and fast dissolution rate without appreciable reduction in mechanical properties were obtained. This concentration was considered to be the optimum for use of calcium chloride as an additive in chloroquine phosphate tablets containing gellan gum.

Key words: Gellan gum, granulating agent, chloroquine phosphate, calcium chloride

INTRODUCTION

Binders confer structural strength required by tablets during processing, handling, packaging and transportation. They used to impart cohesion and improve fluidity and compressibility of powders. Adhesives deform plastically during compression and are forced into the particulate space where they increase the area of contact between particles and form strong solid bonds whose strength depends on the nature and amount of binder employed (Odeku and Itiola, 2005).

Substances classified as natural gum; semi-synthetic polymers and waxes have been used as adhesives or granulating, suspending or emulsifying agents in both solid and liquid dosage formulations (Odeku and Itiola, 1998; Nasipuri *et al.*, 1999; Odeku and Itiola, 2002; Odeku, 2005; Emeje *et al.*, 2006; Jon *et al.*, 2006). These gums have been used in producing tablets with different mechanical strength, consolidation and drug release properties for different pharmaceutical purposes. These gums are generally no-toxic and widely available, hence the continued interest (Odeku and Itiola, 2005). Granulating agents can be incorporated in two ways; as a powder in dry granulation process, it enhances the adhesion of direct compression formulations and is termed pressure binder and as mucilage in wet-granulation process, it is termed solution binders (Krycer *et al.*, 1983). Granulating agent efficiency as shown by tablet strength and friability is influenced by the adhesive solution, formation and deformation behaviour of the granulating film, cohesion pressure of the adhesive film, cohesive pressure of the granulating agent powder and the pressure of the granulating agent.

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Gellan gum is an anionic microbial polysaccharide aerobically fermented by the bacterium *Sphingomonas elodea* (Rath and Schmidt, 2001; Emeje *et al.*, 2007b). It contains glucose glucuronic acid and rhamnose in the molar ratio 2:2:1 as a linear tetrasaccharide repeat unit. It is partially acylated with acetyl and L-glycerol groups located on the same glucose molecule, which do not interfere with double helix formation, but alters its ion bonding ability, hindering chain association and this account for the change in texture brought about by de-etherification. It has the characteristic property of temperature –dependent and cation-induced gelation (Fukada *et al.*, 2002). It forms gel with a range of textural properties from soft and elastic on one extreme to hard and brittle at the other. One of the most important features of a gelling agent is the texture it provides. A technique known as, Texture Profile Analysis (TPA) has been used to quantitatively describe the texture of gellan gum gels which includes, hardness, modulus, brittleness and elasticity. These properties make it suitable as a structuring and gelling agent in the food industry, an alternative to agar in microbiological media, plant tissue cultures and as an additive in toothpaste and deodorants. More recently, the ability of gellan gum to gel in the presence of cations has made it useful in the bioencapsulation of biodegradable substances such as enzymes, by the ionotropic gelation method (Brahma and Kwon, 2005). The addition of a gel-promoting cationic salt solution to the hot gum at 80- 90°C before cooling to ambient temperature produces a demouldable gel by association of the fibrils, with gelation depending on the type and strength of ions and with divalent ions being more effective than the monovalent ions (Alhaique *et al.*, 1995; Brahma and Kwon, 2005).

In the present study, gellan gum was evaluated for its granulating/adhesive properties in a chloroquine Phosphate based formulation. The effect of a divalent cation, calcium chloride on its adhesion and other mechanical properties of the tablets were also investigated.

MATERIALS AND METHODS

Materials

Gellan gum (Kelco USA), chloroquine phosphate, maize starch, gelatin, lactose, (BDH) Ltd., Poole, England), calcium chloride, (May and Baker England), sodium starch glycolate (Generichem, Little falls, New Jersey, USA) magnesium stearate (Amend Drugs and Chemicals, Irvington, New Jersey, USA). All other reagents used were of analytical grade and were used as purchased or obtained from their manufacturers.

Methods

Preparation of Chloroquine Phosphate Granules

We dry-mixed 300 g batches of a basic formulation of chloroquine phosphate (83.33% w/w), sodium starch glycolate (6% w/w) and Lactose (9.67% w/w) for 5 min in a tumbler mixer (karl kolb, Dreieich, West Germany). The batches were then moistened with 30 mL of gelatin or starch mucilage or appropriate amounts of gellan gum solution to produce samples containing various concentrations of gellan gum. Massing was continued for 5 min and the wet masses were granulated by passing them a 1.00 mm sieve. The granules were dried in a hot air oven at 60°C for 24 h, resieved through a 0.6 mm sieve and then mixed with 1% w/w magnesium stearate. The degree of mixing of the granules was then determined by spectrophotometric assay of chloroquine phosphate at 343 nm and was found to be > 0.97.

Preliminary investigation revealed optimum performance of gellan gum as a granulating agent / adhesive in chloroquine phosphate tablets at 2.5% w/w. Consequently five batches of chloroquine phosphate tablets were produced to contain a mixture of 2.5% w/w gellan gum and calcium chloride in the concentration range of 0.1 to 0.5% w/w.

Evaluation Tests on Chloroquine Phosphate Granules

Particle Size Analysis

The particle size analysis was done using the method of sieving (Endecott's Ltd., UK).

True Density

The true densities were determined using pycnometer method with ether as displacement fluid.

Flow Properties

Angle of Repose

The dynamic angle of repose, θ and flow rate were determined using the fixed funnel method.

Bulk and Tapped Densities

The bulk and tapped densities were determined by pouring the 500-1000 μm size fractions of granules at an angle of 45° through a funnel into a glass measuring cylinder with a diameter of 22 mm and a volume of 50 mL (Emeje and Kunle, 2004). The ratio of the mass of the granules before and after tapping was taken as the bulk and tapped densities, respectively.

Hausner Quotient, Compressibility Index and Granule Porosity

Hausner quotient, Compressibility Index (C %) and Granule Porosity were calculated from the following equations:

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Poured density}} \quad (1)$$

$$\text{Compressibility} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100\% \quad (2)$$

$$\text{Granule Porosity, } e = 1 - \delta_b/\delta_t \times 100 \quad (3)$$

Packing Characteristic by Kawakita Model

The characteristics of packing of powder solids, changes in bulk volume by tapping and the relationship between the compressibility, fluidity and cohesion of various chloroquine phosphate batches were investigated. A 20.0 g quantity of each batch was poured into a 50 mL glass cylinder. The heap was leveled by a little tap and the bulk volume V_0 , accurately measured. The cylinder was then mechanically tapped by dropping repeatedly through a height of 1 cm at the rate of 15 drops min^{-1} until no further volume reduction was observed. Values for the volume changes of the powder column V , after various numbers of taps were recorded as an average of six determinations. The degree of volume reduction represented by compatibility C , was calculated from the changes in volume.

$$C = (V_0 - V)/V \quad (4)$$

Compatibility which involves compression and consolidation was used to determine the densification of the powder solid using kawakita model (Emeje *et al.*, 2007) represented as Eq. 5.

$$N/C = N/a + 1/ab \quad (5)$$

Where,

a = Represents compatibility constant, which describes the degree of volume reduction at limit of tapping.

1/b = Represents the constant related to cohesion and is called cohesiveness. To obtain numerical values for constants a and 1/b.

N/C = Versus N were plotted and values extrapolated from slope (1/a) and intercept 1/ab.

Compression of Granules and Evaluation of Chloroquine Phosphate Tablets

Three hundred milligram compacts were made at a pressure setting of 50 units in an F-3 Manesty single punch tableting machine fitted with flat-faced punches. Compacts were properly stored in airtight specimen bottles and allowed to equilibrate for 24 h before further evaluations.

Tablet Dimensions

The thickness and diameter of compacts of the chloroquine phosphate tablets were determined using a micrometer gauge (Mitutoyo, Japan). The mean and standard deviation of twenty randomly selected tablets from each batch was calculated.

Uniformity of Weight

The weight of twenty randomly selected tablets from each batch of chloroquine phosphate tablets were determined individually and collectively. The mean weight and standard deviation were computed. The percentage coefficient of tablet weight variation (CV) was calculated using; Eq. 6:

$$CV = \frac{\text{Standard deviation}}{\text{Mean weight}} \times 100 \quad (6)$$

Crushing Strength

The Erweka (GmbH, Germany) hardness tester was used to determine the force required to diametrically break ten randomly selected tablets from each tablet batch.

Friability

Ten tablets selected randomly from each tablet batch were dedusted and weighed using analytical balance. These were introduced into a friabilator (Erweka, GmbH, Germany), which was set to rotate at 25 ± 1 rpm for 4 min. At the end of the rotation time, tablets were dedusted, re-weighed and the percentage weight loss calculated as the friability.

Binding Capacity

The binding capacity of each tablet batch was calculated as the ratio of mean crushing strength to mean thickness, expressed in kg f mm^{-1}

$$\text{Binding capacity} = \text{Mean crushing Strength} / \text{Mean thickness} \quad (7)$$

Disintegration Time

The disintegration times of six randomly selected tablets from each tablet batch were evaluated in 0.1 N hydrochloric acid at $37 \pm 1^\circ\text{C}$ using Erweka disintegration apparatus. The BP (2004) method without disk was adopted. The time for each tablet to completely disintegrate and pass into solution was noted and mean value and standard deviation calculated.

Dissolution Profile Studies

The dissolution profiles of two tablets from each tablet batch were determined individually in 1000 mL of 0.1 N hydrochloric acid, maintained at 37±1°C using Erweka dissolution rate testing unit according to the USP (2004) paddle method II at a rotating speed of 50±1 rpm. A five-milliliters sample was withdrawn at predetermined time intervals and replaced with equal volume of the dissolution medium. The absorbance of the chloroquine phosphate in the samples were determined spectrophotometrically in a Spectronic 21D (Milton Roy model) at the wavelength of 343 nm. Calibration curves (Beer's plots) for chloroquine phosphate was prepared from a pure sample of the drug. The percentage of drug released after specific time intervals were calculated with reference to the absolute drug contents. The dissolution profile curves of percentage drug dissolved against time in minutes were then plotted. Dissolution parameters T_{50%} and T_{70%} were used to express the time taken for fifty and seventy percent of the drug respectively to be released.

Statistical Analysis

The data obtained were analysed using Microsoft Excel software (SSPS) which included mean, standard deviation variances and ANOVA (F-test) at p<0.05 level of significance.

RESULTS AND DISCUSSION

Micromeritic Properties of Chloroquine Phosphate Granules

Results show that the granules sizes were predominantly in the range of 0.49 to 0.54 mm (Table 1). Gellan gum produced granules comparable to those of reference granulating agents (gelatin and maize starch Mucilage). Chloroquine phosphate granules containing gellan gum were larger in size than those of gelatin and maize starch. This may probably be due to the relatively high adhesive property of gellan gum compared to gelatin and maize starch mucilage. The bulk and tapped densities and the porosity of the granules containing gellan gum were not too different from those containing maize starch mucilage and gelatin. Granule porosity significantly controls densification and deformation during compression as well as compaction, which is measured by tensile strength (Summers, 1999). The highest porosity value of 77.13% was obtained for granules containing 5.0% gellan gum. This is believed to encourage increased deformation and densification yielding highly compressible granules (Summers, 1999). Ian *et al.* (1982) reported that high intragranular porosity results in increased granule strength and subsequent bonding within the compact, which will reflect as increased crushing strength. This probably explains why the tablets made from granules containing 5% gellan gum have the highest crushing strength. Results from indirect determinations of flow properties; Hausner's quotient and angle of repose which are measures of interparticulate friction, recorded the highest values at all concentrations of gellan gum, implying a stronger interparticulate friction within the granules.

Table 1: Micromeritics properties of chloroquine phosphate granules

Binder conc. (%)	Bulk density	Tapped density	Granule density	Granule porosity (%)	Hausner quotient	Angle of repose (o)	Carr's index	Flow rate (g sec ⁻¹)	Mean PS (mm)
	-----	(g m ⁻³)	-----						
Control	0.597±0.009	0.714±0.000	2.326	74.33	0.197	39.10±0.516	16.4	4.64±0.32	0.478
Gellan									
2.5	0.602±0.007	0.714±0.000	2.500	75.92*	1.186	35.69±1.432*	15.7	6.67±0.00	0.500
5.0	0.602±0.007	0.714±0.000	2.632	77.13*	1.185	34.85±1.432*	15.7	6.67±0.00	0.519
7.5	0.571±0.000	0.673±0.012	1.887	69.74	1.179	35.55±0.699*	15.3	5.00±0.00*	0.485
Gelatin									
2.5	0.588±0.000	0.683±0.012	1.887	68.83	1.161	33.45±0.567	13.9	5.71±0.00	0.485
5.0	0.571±0.000	0.673±0.012	2.041	72.02	1.179	33.07±0.716	15.2	5.71±0.00	0.533
7.5	0.571±0.000	0.652±0.111	2.000	71.45	1.140	33.25±0.699	12.3	6.67±0.00	0.539
Maize st.									
2.5	0.553±0.006	0.602±0.007	1.639	66.24	1.090	26.82±1.008	8.3	8.00±0.00	0.508
5.0	0.558±0.000	0.689±0.000	2.222	74.89	1.173	31.79±0.316	14.7	6.67±0.00	0.508
7.5	0.513±0.000	0.571±0.000	1.887	72.81	1.114	29.27±1.844	10.3	8.00±0.00	0.521

PS: Particle Size, *: p<0.05

Table 2: Values of cohesiveness and compatibility from the kawakita equation

Binder concentration (%)	Cohesiveness (%)	Compatibility (%)	Carr's index or compressibility (%)
0	14.033	21.588	16.4
Gellan gum			
2.5	13.352	21.463	15.7
5.0	15.109	19.036	15.7
7.5	8.989	20.219	15.3
Gelatin gum			
2.5	11.399	18.479	13.9
5.0	12.604	17.339	15.2
7.5	12.213	14.467	12.3
Maize starch mucilage			
2.5	15.985	7.878	8.3
5.0	9.079	17.981	14.7
7.5	9.896	9.508	10.3

However, the results obtained showed that the granules produced from gellan at all the concentrations investigated flow well. Carr's index and flow rate indicate that granules containing gellan gum had values which compared well with gelatin and maize starch mucilage (Table 1 and 2). The flow properties were found to increase in the order. Maize starch > gelatin > gellan gum.

Cohesiveness and Compatibility

The relationship between N/c and N for chloroquine phosphate granules showed linearity (Table 2). Extrapolations from slope and intercept gave Kawakita constant a (percentage compatibility) and 1/b (cohesiveness) occurring in high ranges from 9.896 to 15.109 and 9.508 to 21.588, respectively. Theoretically, the Kawakita constant for compatibility a that relates to the degree of volume reduction due to tapping should equal Carr's compressibility index. However, results from Table 2 showed that Kawakita constant a was larger than Carr's index. A similar observation has been reported by other authors (Tan and Newton, 1990; Podczech and Sharma, 1996; Emeje *et al.*, 2007a). This lack of correlation, was attributed to the difficulty in attaining the true tapped volume especially at low pressures.

Mechanical Properties of Chloroquine Phosphate Tablets

Granulation of Chloroquine Phosphate with only water produced very soft tablets (2.95±0.4 kgf). The use of gellan gum at concentrations of 2.5 to 7.5% w/w improved bonding properties, increasing hardness above >4 kgf and yielded satisfactorily strong tablets, which did not cap or laminate. Results obtained compared well with gelatin and maize starch. A comparison of mean hardness followed the order gelatin > gellan gum > maize starch. This observation is not unexpected as highly water-soluble polymers such as gellan gum should enhance bonding (Emeje *et al.*, 2007b).

Statistical analysis reveals that the binding effect of gellan gum differed significantly from that of gelatin at 2.5% w/w and from both gelatin and maize starch mucilage at 7.5% w/w. There was no significant deference in its from that of gelatin at 5% w/w. Binding properties of batches from maize starch mucilage did not differ significantly, from those of gellan gum at 2.5 and at 7.5%.

Table 3 shows that the tablets containing no granulating agent had the highest friability and revealed that all concentrations of the granulating agent were effective in improving cohesion and yielding friability results within acceptable limit, (< 1%) (Aulton and Wells, 1999). The friability of the tablets were in the order of control > maize starch > gelatin > gellan gum, showing that gellan gum proved to be a more effective binder than maize starch.

The high tablet porosity recorded by gellan gum (>72.07%), is probably responsible for large pore spaces available for water sorption thereby enhancing rapid ingress into the compact. Table 3 shows marked delay in disintegration time for tablets containing gellan gum probably due to the quick formation of mucilaginous coat around the tablet on wetting. Gellan gum at 5%w/w had the highest

Table 3: Mechanical properties of chloroquine phosphate tablets

Binder conc. (%)	Mean hardness (kgf)	Percent friability (%)	Tablet porosity (%)	Mean disintegration time (min)	Binding capacity (kgf mm ⁻¹)
Control	2.95±0.4	0.368	79.94	17.10±1.2	7.57
Gellan gum					
2.5	6.65±0.7	0.098	77.50	28.33±4.3*	20.28*
5.0	7.95±0.4	0.195	79.44	40.00±1.3*	23.40*
7.5	6.85±0.2	0.130	72.07	34.00±0.3*	19.60*
Gelatin					
2.5	7.85±0.2	0.221	74.35	16.50±1.1	20.13
5.0	8.55±0.4	0.251	74.89	17.50±1.8	23.10
7.5	7.15±0.3	0.128	79.12	15.70±0.8	16.25
Maiz st. mucii					
2.5	5.85±0.2	0.328	67.83	19.00±0.6	16.71
5.0	6.65±0.2	0.293	82.33	22.80±0.7	14.15
7.5	4.95±0.1	0.236	76.70	18.20±1.8	12.69

*: p<0.05

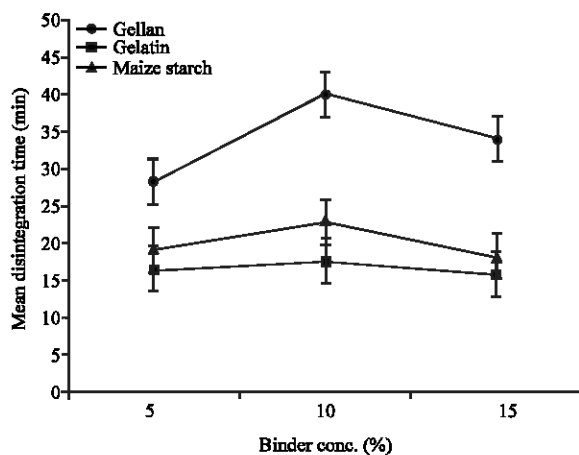


Fig. 1: Effect of binder concentration on disintegration time

binding capacity of 23.4 kg m⁻¹ while the batch without a binder expectedly showed the least value of 7.57. Gellan gum generally compared well with corresponding concentrations of gelatin but proved to be a better binder than maize starch.

Mean Disintegration Time

Table 3 and Fig. 1 showed marked increase in disintegration time with increase in the concentration of gellan gum from 2.5 to 7.5%w/w. The disintegration test result shows that gellan gum at these concentrations prolonged disintegration of the tablets unlike gelatin and maize starch which produced fast disintegrating tablets. The behavior of gellan gum is consistent with the behavior of polymers that gel in contact with fluid (Emeje *et al.*, 2006).

Effect of Calcium Chloride on the Mechanical Properties of Chloroquine Phosphate Tablets Prepared with 2.5% Gellan Gum

Table 4 shows that varying concentrations of calcium chloride significantly altered the mechanical properties of chloroquine phosphate tablets prepared with 2.5% gellan gum. The binding capacity some batches were greatly reduced and this may have resulted in the very weak (<4 kgf) and highly friable (>1%) tablets. At concentration of 0.3%w/w calcium chloride produced tablets with friability value of 14.03%. Tablet porosity increased from 77.5 to 88.76% with a corresponding increase in friability. There was marked decrease in disintegration time from 28.33 to 7.33 min. It was observed

Table 4: Effect of calcium chloride on the mechanical properties of chloroquine phosphate tablets prepared with 2.5% gellan gum

Binder conc. (%)	Mean hardness (kgf)	Percent friability (%)	Tablet porosity (%)	Mean disintegration time (min)	Binding capacity (kgf mm ⁻¹)
Control (25 gellan gum)	6.65±0.700	0.098	77.50	28.33±4.30	20.200
25% Gellan gum+Calcium chloroquine					
0.1	1.75±0.264	1.160	88.76	1223.00±0.26	2869.000
0.2	1.05±0.550	1.070	88.26	8.67±0.07	1.630
0.3	260.00±0.696	14.030	84.22	14.30±0.52	3.719
0.4	4.20±1.229*	0.710	78.07	16.80±0.63*	8.367
0.5	260.00±0.615	1.570	83.27	7.33±0.50	3.852

*: p<0.05

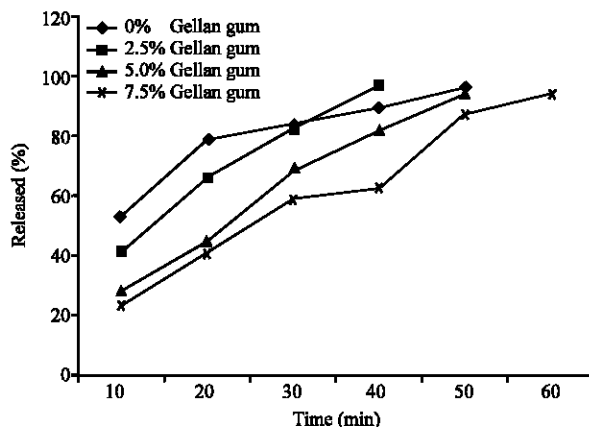


Fig. 2: Effect of concentration of gellan gum on the dissolution of chloroquine phosphate tablets

that 0.4% w/w calcium chloride was the optimum concentration; a point at which disintegration decreased significantly without significant effect on the mechanical properties, hence relatively strong tablets (4.2±1.229 kgf) with acceptable friability (0.71%) and porosity (78.07%) values.

Statistically, an F-ratio of 0.942 and 0.840 was obtained for 0.3 and 0.4% w/w Calcium chloride, respectively. The implication is that the presence of calcium chloride may not alter the mechanical properties of gellan gum in chloroquine phosphate tablets at 0.434 and 0.471 significant Levels respectively. However at 0.2 and 0.5% w/w Calcium chloride Concentrations, F-ratio of 1.350 and 1.033 were obtained indicating a significant difference from the control observed by drastic alteration of the mechanical properties at 0.319 and 0.404 significant levels (Table 3 and 4).

***In vitro* Drug Release**

The release of chloroquine phosphate from all batches containing the granulating agents was delayed when compared to the control batch (without a granulating agent) (Fig. 2-5). The time for release of 50 and 70% (T₅₀ and T₇₀) of chloroquine from the control batch were 4.7 and 8.3 min, respectively compared to T₇₀ of 42.5 min for gellan containing batch (Table 5). As the concentration of maize starch increased in the formulation, there was a noticeable increase in the dissolution rates. However, increased concentration of gellan gum and gelatin resulted in decreased dissolution rates (Table 5). This suggests that gellan gum is a good granulating agent at all concentrations investigated in chloroquine phosphate tablets and compared well with maize starch and gelatin. All the batches showed 70% release of the drug within 45 min as specified in the BP. Gellan gum has the highest T_{50%} (14 to 25.5 min) and T_{70%} (23.0 to 42.5 min) indicating relatively a slower drug release, this is may be due to the high binding capacity and delayed disintegration time probably caused by gel formation within the gel matrix.

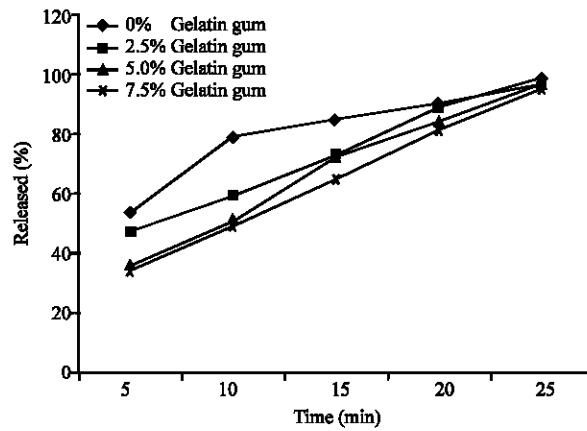


Fig. 3: Effect of concentration of gelatin on the dissolution of chloroquine phosphate tablets

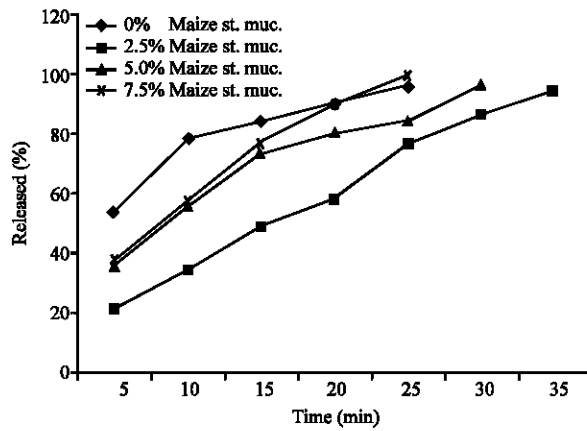


Fig. 4: Effect of concentration of maize starch on the dissolution of chloroquine phosphate tablets

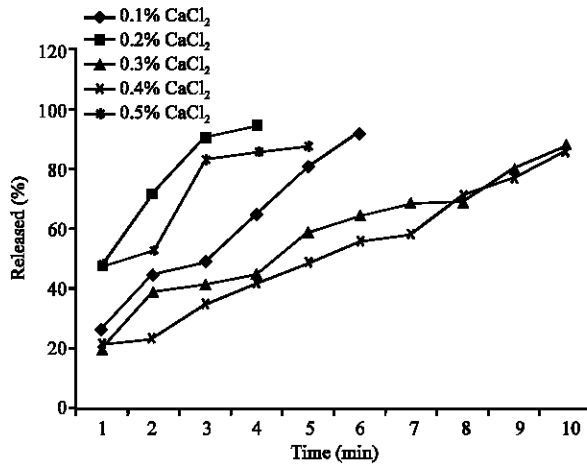


Fig. 5: Effect of calcium chloride on the release profile of chloroquine phosphate containing gellan gum

Table 5: Dissolution parameters of chloroquine phosphate tablets

Binder conc. (%)	T ₅₀ (min)	T ₇₀ (min)
Control	4.7	8.3
Gellan gum		
2.5	14.0	23.0
5.0	22.0	31.5
7.5	25.5	42.5
Gelatin		
2.5	7.4	14.4
5.0	10.0	14.7
7.5	10.4	16.8
Maize starch		
2.5	15.5	23.0
5.0	8.5	13.5
7.5	8.0	14.3

Table 6: Effect of calcium chloride on the dissolution of chloroquine phosphate tablets

Binder conc. (%)	T ₅₀ (min)	T ₇₀ (min)
Gellan gum 2.5	13.77	23.3*
CaCl ₂ 0.1+Gellan 2.5	3.00	4.2
CaCl ₂ 0.2+Gellan 2.5	1.10	1.8
CaCl ₂ 0.3+Gellan 2.5	4.30	6.7
CaCl ₂ 0.4+Gellan 2.5	5.00	7.7
CaCl ₂ 0.5+Gellan 2.5	1.10	25.0

*: p<0.05

The presence of calcium chloride increased the rate of drug release as can be seen from the drastic reduction in T₅₀ and T₇₀ values from 13.17 and 23.3 min, respectively to ≤5.0 and ≤7.7 min, respectively (Table 6). It was observed that unlike batches without calcium chloride, all the batches containing calcium chloride had achieved complete drug release within 10 min. 0.4% w/w calcium chloride was discovered to be the optimum concentration.

CONCLUSION

This study has proven that gellan gum could be an efficient granulating agent in the preparation of Chloroquine phosphate tablets as it compared well with standard granulating agents such as gelatin and maize starch. The presence of calcium chloride decreased the mechanical properties of chloroquine phosphate tablets and at 0.4% w/w calcium chloride; there was a reduction in disintegration time of the tablets without any deleterious effect on their mechanical properties. This concentration was considered optimum for calcium chloride as an additive in tablet formulations containing gellan gum.

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