The Binder Effect of Povidone on the Mechanical Properties of Paracetamol Containing Tablets

E.K. NJEGA[1]*, S.M. MARU[2] AND L.J. TIROP[2]

[1]*Department of Pharmacy, Meru Teaching and Referral Hospital*
[2]*Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi*

ABSTRACT

Anecdotal evidence from the pharmaceutical industry suggests that the formulation of paracetamol tablets is problematic due to unsatisfactory mechanical properties. Thus the choice of a binder is a critical material attribute in the formulation of these tablets. This study evaluated the binder effect of povidone K90 and povidone K30, differing in degree of polymerization, on the mechanical properties of paracetamol tablets. Five batches of paracetamol tablets with varying binary binder ratios of povidone K90 and povidone K30 were formulated, maintaining a total binder concentration of 5%w/w per tablet. The binary binder ratios of povidone K90: povidone K30 were 1:0, 3:1, 1:1, 1:3 and 0:1 in tablet batches B1, B2, B3, B4, and B5 respectively. The mechanical properties of the resultant tablets were evaluated using the crushing strength friability ratio, as the response variable for tablet strength, and the crushing strength friability ratio disintegration time, as the response variable for tablet quality. Batch B1 tablets had the highest crushing strength friability ratio whilst batch B4 tablets had the highest crushing strength friability ratio disintegration time, $p<0.05$, 95% confidence level. Formulation of tablets with a 1:3 ratio of povidone K90: povidone K30, produced tablets with the best mechanical properties demonstrating both sufficient crushing strength and optimal disintegration time.

Keywords: paracetamol tablets, povidone, crushing strength, friability, disintegration

INTRODUCTION

Binders are agents used to impart cohesiveness to powdered material during the formulation of granules and/or tablets. Immobile liquid binders affect the type of granules produced not only in the mechanism of agglomeration but also by their distribution within the agglomerate [1]. Material with low or no cohesiveness will require a stronger binder than materials with high cohesiveness. Binders routinely used in tablet formulation may be natural (e.g., acacia gum, tragacanth) or synthetic (e.g., hydroxylpropylmethylcellulose, povidone). The choice and concentration of the binder for tablet manufacture is carefully selected during preformulation studies.

Paracetamol crystallizes in three polymorphic forms; monoclinic form I (stable), orthorhombic form II (metastable) and the unstable form III [2]. The monoclinic paracetamol form I, is the thermodynamically stable form [3], which is commonly used in the manufacture of tablets. Paracetamol form I cannot be compressed directly due to poor densification properties, necessitating the wet granulation process prior to compression. Furthermore, paracetamol exhibits elastic deformation on compression; a reversible phenomenon hindering tablet formation. These characteristics predispose paracetamol tablets to capping, a troublesome tablet defect.

The present investigation will determine the mechanical properties of the tablets formulated with varying ratios of povidone K90 and povidone K30 as binder, at a 5%w/w total concentration of binder per tablet. Povidone is a synthetic polymer with different grades varying in degree of polymerization, hence molecular weight which may be expressed as viscosity dependent K-values for example K12, K15,

*Author to whom correspondence may be addressed. Email: kithinjii@yahoo.com

K17, K25, K30, K60, K90 and K120. Povidones with K-values equal to or below 30 occur as spheres whilst those with K values of 90 or above occur as plates. Selection of povidone K30 and K90 for this study will allow elucidation of the effects of these polymers of differing characteristics on the mechanical properties of the resultant tablets.

MATERIALS AND METHODS

Materials

The raw materials, all of pharmaceutical grade, namely Paracetamol powder BP (Changushuhaugang Pharmaceutical Co. Ltd. YuaiangYetangChangshu City Siangsu province, China), white corn starch BP (BDH chemicals Ltd. Poole, England), magnesium stearate BP (Sigma Aldrich Co. Spruce street St. Louis Missouri, U.S.A), potassium sorbate BP (Rugaochingjiangfood Co. Ltd. Tonggang road Changjiang town, Rugao city Jinangsu, China) and povidone K90, povidone K30 (BASF SE Carl Bosch street Ludwigshafen, Germany) were received as a donation from Lab and Allied Company, Nairobi, Kenya.

Equipment

The equipment employed in this study included a planetary mixer, tablet press (Erweka electric type, Germany), disintegration test machine (Erweka 2T3 GmbH Heusentamm, Germany), friability tester (ErwekaHeusentamm type TA3R, Germany) and hardness tester (Schleuniger mod 2E/205, Switzerland).

Preparation of dry powder blend

A 300g dry powder blend comprising of paracetamol (85%w/w), corn starch (13%w/w) and potassium sorbate (1%w/w) was prepared.

Preparation of granules

The wet granulation method of massing and screening was used. The 300g dry powder blend of paracetamol (85%w/w), corn starch (13%w/w) and potassium sorbate (2%w/w) was split into five batches. A 5%w/w binder concentration, made of binary mixtures of povidone K90 and povidone K30 in the ratios of 0:1, 1:3, 1:1, 3:1 and 1:0, was added and mixed in dry form to the five batches B1-B5 (Table 1). The batches were massed with the similar appropriate amounts of distilled water for 5 minutes. Granulation end point was determined by visual inspection. The wet mass was forced through a 710µm sieve and dried in a hot air oven at 50˚C for 70 minutes. The dried granules were passed through a series of sieves of sizes 710µm, 355µm and 180µm to obtain granules of different sizes. 20% of the fines were reintroduced into the sieved granules. The sieved granules were lubricated with 1%w/w magnesium stearate prior to compression.

Table 1: Tablet master formula (concentration given in %w/w, with mg in parenthesis)

No.	Material	B1	B2	B3	B4	B5
1	Paracetamol	80.00 (300mg)	80.00 (300mg)	80.00 (300mg)	80.00 (300mg)	80.00 (300mg)
2	Corn starch (disintegrant)	13.00 (48.75mg)	13.00 (48.75mg)	13.00 (48.75mg)	13.00 (48.75mg)	13.00 (48.75mg)
3	Potassium sorbate (preservative)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)
4	**PVP K-30 (binder)**	**0.00 (0.00mg)**	**1.25 (4.69mg)**	**2.50 (9.37mg)**	**3.75 (14.06mg)**	**5.00 (18.75mg)**
5	**PVP K-90 (binder)**	**5.00 (18.75mg)**	**3.75 (14.06mg)**	**2.50 (9.37mg)**	**1.25 (4.69mg)**	**0.00 (0.00mg)**
6	Magnesium stearate (lubricant)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)	1.00 (3.75mg)
7	Total	100 (375mg)	100 (375mg)	100 (375mg)	100 (375mg)	100 (375mg)

Compression of granules

Granules of size fraction 710µm - 180µm were used to prepare 375mg± 15mg tablets using a single, electric tablet press iEP-1 (Erweka Germany) fitted with 10mm flat punch and die set. A fixed compression load was determined during pre-trials and thereafter used throughout compression.

Post-compression tests of tablets

The resultant tablets were evaluated for uniformity of weight, disintegration time, crushing strength and friability.

Uniformity of weight

Twenty tablets were picked at random and individually weighed. The percentage deviation of individual tablet weight from the average weight was determined.

Disintegration test

Tablet disintegration was determined in distilled water at 37±0.5˚C in a six unit disintegration unit (Erweka 2T3, GmbH Heustentamm, Germany). Tablets were placed on the wire mesh just above the surface of the distilled water in the tube. The time taken for each of the tablets to disintegrate and all the granules to go through the mesh was recorded.

Crushing strength test

A Schleuniger hardness tester (mod 2E/205, Switzerland) was used to determine the load required to diametrically break the tablet into two halves. The mean of five readings was taken.

Friability test

The friability of the tablets was determined by a friability test machine (Erweka, Heusentamm type TA3R, Germany) operated at 25 revolutions per minute for 4 minutes. Twenty tablets were selected at random and their total weight taken before and after friability testing. The percentage weight loss, friability, was determined.

RESULTS AND DISCUSSION

The results obtained for the various tests are presented in Table 2.

Table 2: Evaluation of tablet quality

PARAMETER	B1	B2	B3	B4	B5
5%w/w binder ratio K90: K30	1:0	3:1	1:1	1:3	0:1
Tablet thickness(mm) ±SD n=3	4.11±0.05	4.10±0.07	3.95±0.04	3.90±0.08	4.00±0.10
Tablet diameter (mm) ±SD n=3	9.93±0.01	9.92±0.01	9.94±0.03	9.92±0.02	9.95±0.01
Uniformity of weight(mg) ±SD	390±0.01	380±0.01	380±0.01	370±0.01	380±0.01
Crushing strength (kgf) ±SD	9.08±0.81	9.12±1.27	12.88±0.94	11.36±0.82	13.00±0.14
Friability(%) ±SD n=3	0.34±0.14	0.88±0.08	0.69±0.08	0.91±0.08	1.05±0.14
Crushing strength/FriabilityRatio (CSFR)	26.71	10.36	18.67	12.48	12.38
Disintegrationtime(min) ±SD n=3	99.55±16.56	30.74±18.20	14.97±5.81	2.51±0.77	4.10±1.22
Crushing strength friability ratio: Disintegration time (CSFR:DT)	0.26	0.33	1.24	4.97	3.01

The tablet diameter and thickness was consistent throughout the five tablet batches, with all batches passing the uniformity of weight test. All tablet batches passed the friability test with the exception of tablet batch B5.

The official disintegration time for uncoated tablets is less than 15 minutes. Batches B1 and B2 had disintegration times of 99.55 minutes and 30.74 minutes respectively. Batches B3, B4 and B5 had disintegration times of 14.97 minutes, 2.51 minutes and 4.10 minutes respectively. Batches with higher amounts of povidone K90 had longer disintegration times. This implies that povidone K90 had a higher binding capacity than povidone K30.

Crushing strength/friability ratio (CSFR) has been used as an index of the mechanical strength of tablets [4], with high CSFR values indicating stronger tablets. Batch B1 tablets with 100% povidone K90 binder presented the highest CSFR of 26.71 while batch B5 containing 100% povidone K30 binder had a CSFR of 12.38 (Figure 1). This confirms the earlier observation that povidone K90 has a higher binding capacity than povidone K30.

Crushing strength friability ratio/disintegration time ratio (CSFR/DT) has been suggested as a better index than CSFR in measuring tablet quality. In addition to measuring tablet strength (crushing) and weakness (friability), it also evaluates the negative effects of these parameters on disintegration time. Higher CSFR/DT values indicate a better balance between binding and disintegration properties [5]. Batch B4 had the highest CSFR/ DT ratio of 4.97. The order of CSFR/DT in ranking amongst batches was B4>B5>B3>B2>B1 (Figure 2).

The results indicate that batches with the highest mechanical strength as measured by the crushing strength/friability ratio (CSFR) are not necessarily those with the highest index of tablet quality as measured by the crushing strength friability ratio/disintegration time ratio (CSFR/DT).

Statistical analysis of the results involved the modelling for crushing strength friability ratio (CSFR) and crushing strength friability ratio:disintegration time (CSFR/DT) using R statistical software v. 3.2.0 (Tables 3 and 4).

The above model shows that batch B1 had the highest crushing strength friability ratio (highest coefficient=26.7 and t=41.37 P<0.0005). The model was fitted and it was statistically significant (adjusted R^2=0.9466, P<0.0005). The residuals were normally distributed with a mean of zero and a constant variance. Figure 3 re-emphasizes the regression model findings.

The model on crushing strength friability ratio:disintegration time indicated that batch B4 had the best mechanical property since it had the highest regression coefficient 5.52, t=9.615 and P<0.0005. Batch B1 had the lowest coefficient of 0.2505. However, the p value of 0.5442 was not statistically significant therefore the conclusion of batch B1 having the worst mechanical property cannot be made. The model was fitted, was statistically significant (adjusted R^2=0.8402, P<0.0005) and all the residuals were normally distributed with a mean of zero and a constant variance. Figure 4 maps up the model trends.

Table 3: Modelling for crushing strength friability ratio (CSFR)

FORMULATION/MODELS	Coefficients	Standard error	t value	Pr(>|t|)
B1	**26.7059**	0.6456	**41.366**	P<0.0005
B2	-16.3422	0.9130	-17.899	P<0.0005
B3	-8.0392	0.9130	-8.805	P<0.0005
B4	-14.2224	0.9130	-15.577	P<0.0005
B5	-14.3249	0.9130	-15.690	P<0.0005

R^2=0.955 Adjusted R^2=0.9466, F=107.3, 95%, p<0.005

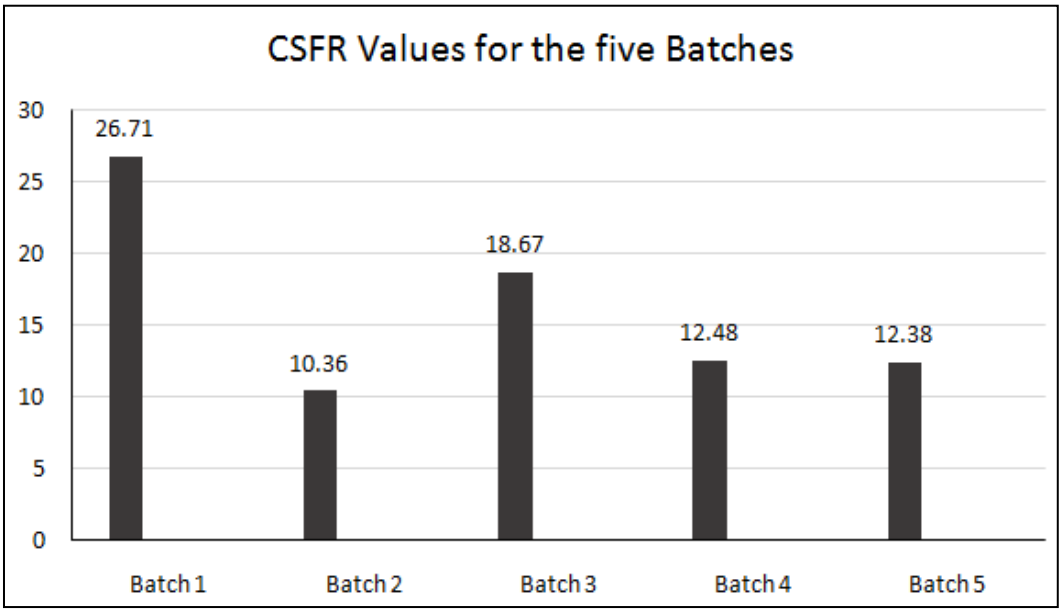

Figure 1: Trend of CSFR values amongst the five tablet batches

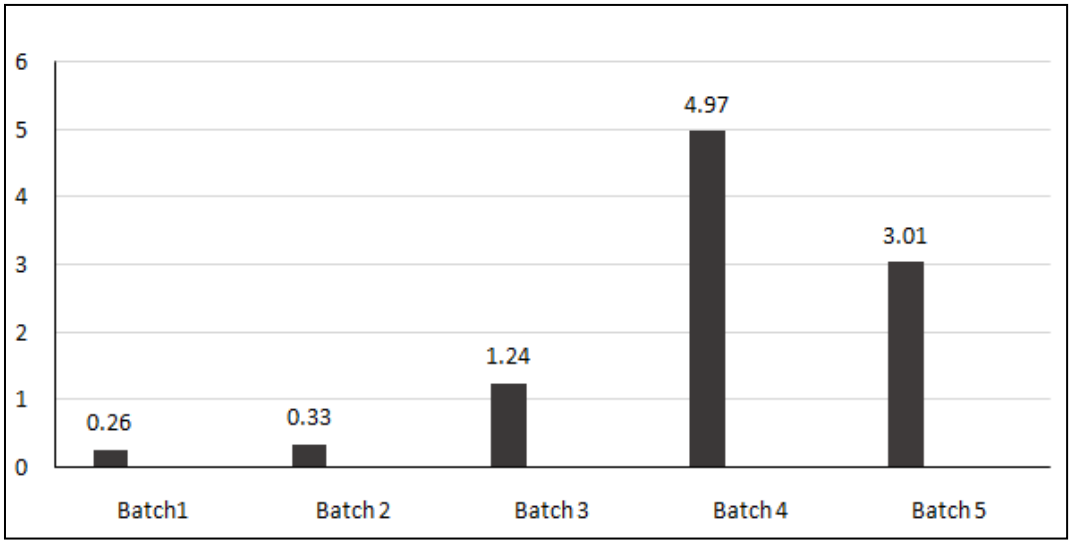

Figure 2: Trend of CSFR/DT values amongst the five tablet batches

Table 4: Modelling for crushing strength friability ratio/disintegration time (CSFR/DT)

FORMULATION/MODELS	Coefficients	Standard error	t value	Pr(>|t|)
B1	0.2505	0.4059	0.617	P=0.5442
B2	0.2518	0.5741	0.439	P=0.6657
B3	1.3138	0.5741	2.289	P=0.0331
B4	**5.5200**	0.5741	**9.615**	**P<0.0005**
B5	3.2505	0.5741	5.662	P<0.0005

R^2=0.8669 Adjusted R^2=0.8402, F=32.56, 95%, p<0.0005

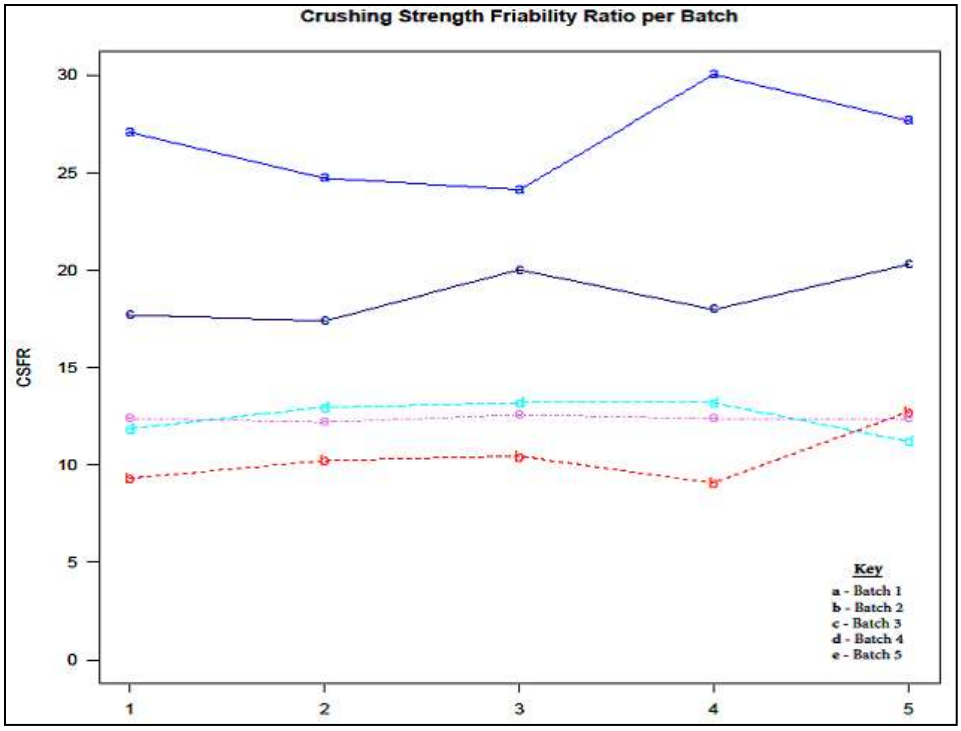

Figure 3: Model fittings for crushing strength friability ratio (CSFR)

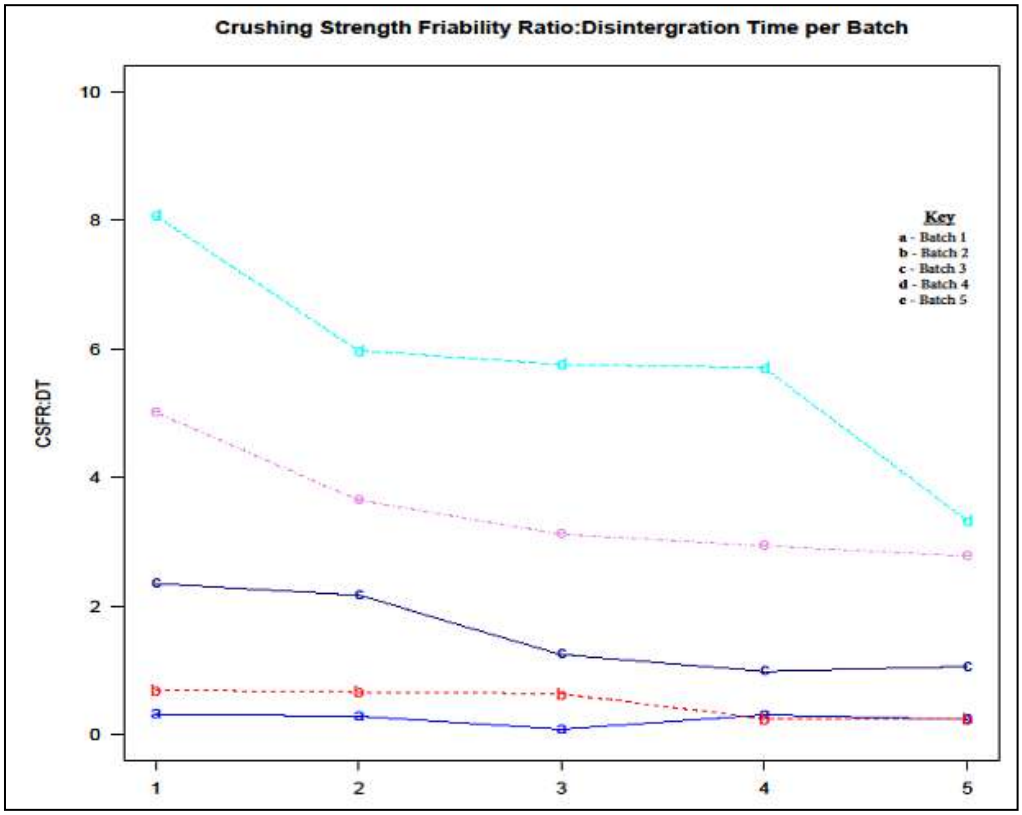

Figure 4: Model fittings for crushing strength friability ratio/disintegration time (CSFR/DT)

CONCLUSION

Batch B1 tablets (povidone K90: povidone K30 of 1:0) had the highest mechanical strength ($p<0.005$) displaying the highest coefficients in the modelling for crushing strength friability ratio. This means that povidone K90 has the highest binding power. Batch B4 tablets, with a povidone K90: povidone K30 binder ratio of 1:3, had the best mechanical property ($p<0.0005$) portraying the highest coefficients in the modelling for crushing strength friability ratio to disintegration time. The results suggest that a binary binder mixture of povidone K90 and povidone K30 in the ratio of 1:3 results in paracetamol tablets with both sufficient crushing strength and optimal disintegration time.

REFERENCES

[1] A. Pandeya. Relating mechanical properties of dry and granulated pharmaceutical powder formulations with tablet quality parameters. The Pennsylvania State University, 2009, pp 11-20.

[2] K. Srinivasan. Int. J. Chem Tech Res. 6, 2014, 1630–1632.

[3] P. Bashpa. Int. J. Chem. Stud. 1, 2014, 25-29.

[4] M. Autamashih, A.B. Isah, T.S. Allagh and M.A. Ibrahim. J. Appl. Pharm. Sci. 1, 2011, 118–122.

[5] M. Femi-Oyewo, T. Ajala and D. Babs-Awolowo. J. Appl. Pharm. Sci. 5, 2015, 043–050.