Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(4):237-242
(http://derpharmachemica.com/archive.html)

Effects of Binder on the Physico-chemical Properties and the Quality of Paracetamol Tablets

[*1]Sunethra K. Gunatilake, [2]Sethsiri S. Samaratunga and [2]Folahan A. Adekola

[1]Department of Natural Resources, Sabaragamuwa University of Sri Lanka, Sri Lanka
[2]Department of Chemistry, University of Ilorin, Ilorin, Nigeria

---

ABSTRACT

A laboratory study was done to evaluate the effects of binder on the physico-chemical properties and the quality of paracetamol tablets prepared by the wet granulation method using three different binders, namely, polyvinyl pyrrolidone (PVP), starch paste and gelatine solution. Tablets were evaluated for uniformity of weight and drug content, hardness & tensile strength, friability, disintegration time and dissolution rate. Results indicated that tablet weights measured for formulation 1, 2 & 3 were well within the ranges, (253.5 ± 12.7), (230.2 ± 17.3) and (238.1 ± 17.9) according to BP standard, respectively. Hardness, tensile strength, and disintegration time evidenced that the gelatine solution appeared to be the best for paracetamol tablet than PVP and starch paste. Friability and dissolution rates were not in agreement with other parameters. It was found that the strength of inter- and intra-granular forces plays key role in maintaining quality of tables. All parameters are dependent on the type, quality, concentration and degree of spreading of a binder.

Keywords: PVP, Starch, Gelatine, Paracetamol tablet, Evaluation Parameters

---

INTRODUCTION

More than 70% of drug dosage forms are formulated in the form of tablets because of their greatest dose precision, stability, low cost and large scale production, various drug release mechanisms, easy transportation and patient compliance. Among the main ingredients mixed with the drug when formulation tablet dosage form, binder plays an important role in achieving the desired quality of the tablets. There are mainly three types of binders namely, sugars, natural, and synthetic/semi-synthetic polymers that can be used in tablet formulation. They may be added either dry or in solution to the tablets prepared by wet granulation. They convert the powder into granules that possesses good flow property and compactability and promotes cohesiveness. Flow property is important to produce tablets with consistent weight and uniform strength. Compactability is important to form a stable and intact compact mass. Physico-chemical properties and the quality of tablet depend on the type, quantity and the way the binder is added. Therefore, the choice of a binder is extremely important in determining final tablet performance.

Therefore, considerable researches have been done to investigate the effects of binder on the quality of the tablets. Researchers have paid attention on the different subject areas to be investigated to evaluate effect of binder on the tablet performance such as fundamental physico-chemical properties of binder itself [1, 2, 3], binder-substrate interaction [4, 5], binder spreading ability [6], solution binders [7], natural binders [8, 9], the effects of binder on bulk density and compactability [10], toughness and flowability[11], and the correlation between dissolution and disintegration rate constants [12].

The aim of this laboratory study is to investigate the effects of binder on the physico-chemical properties and the quality of the paracetamol tablets prepared by wet granulation method. To achieve this end, studies were conducted using three different binders namely, polyvinyl pyrrolidone (PVP), starch paste and gelatine solution. PVP was

added dry in preparing wet mass. Effects of binders were assessed by testing weight variation tolerance, uniformity in drug content, hardness and tensile strength, friability, friability, disintegration time and dissolution studies.

MATERIALS AND METHODS

Materials: Paracetamol (Acetaminophen) was taken as the drug. Lactose was used as diluent. The binder materials investigated were polyvinyl pyrrolidone (PVP), corn starch paste and gelatine solution (acacia mucilage). Magnesium stearate was used as lubricant. Corn starch (dry) and Talc were used as disintegrant and glident, respectively. All these materials were analytical grade and purchased from Scharlau Chemicals.

Apparatus: Micro pipette, Electronic Balance (Sartorius), Heater, No.12 (710mm) and 60 meshes, Oven, Dissolution test station (SR8PLUS – Hanson Virtual Instrument), Disintegration Test System (QC – 21), Tablet Hardness Tester, Friabulator, and UV/VIS spectrophotometer (HEλIOS – Thermo Spectronic)

Preparation of Calibration Curve for Paracetamol
Paracetamol stock solution (100ppm): A stock solution was prepared by dissolving 10mg of Paracetamol in water in a 100ml volumetric flask. The solution was diluted upto the marked level.

Standard Solutions for Calibration: Standard solutions at various concentrations (0.5, 1, 2, 3, 4, and 5 µg/ml) were prepared using the stock solution. Pipetted 0.5, 1, 2, 3, 4, and 5 ml of stock solution into six 10ml volumetric flasks and each of flasks were diluted with deionized water upto the marked level. Then from each of these flasks, 1ml of solution was taken out by using 1000 µl micro pipette and transferred into a 10ml volumetric flask separately and diluted with deionized water upto the mark. UV/Vis absorption was measured at wavelength of 243nm for each solution concentrations and calibration curve was prepared [Plotted Absorbance *vs*. Concentration (µg/ml)].

Preparation of Starch Solution(10% w/w): Weighted 11.25g of Corn Starch into a 250ml beaker, added 112.5ml of water and mixed well while heating at 36° C until the starch dispensed well in the solution.

General Procedure: Preparation of Dry Granules: Paracetamol tablets containing 100mg of paracetamol were prepared using three different binders according to the following 3 formulations.

Formulation No.1: Weighted 50g of paracetamol, 11.25g of polyvinyl pyrrolidone (PVP), 30.875g of lactose and 10.8125g of corn starch and dry-mixed using motor and pestle for about 5 minutes. The powder mixture was blended by tumbling for 10 minutes. The blended mixture was moistened by slowly addition of alcohol to proper wetness and then kneaded well. The wet mass was screened through No.12 mesh (710mm) to prepare small granules. The granules were dried at 50° C overnight in an oven and screened through a No.20 mesh.

Formulation No.2: Weighted 50g of paracetamol, 30.875g of lactose and 10.8125g of corn starch and dry-mixed using motor and pestle for about 5 minutes. The dry powder mixture was blended by tumbling for 10 minutes. The blended mixture was moistened by slowly addition of 10% starch solution to proper wetness and then kneaded well. The wet mass was screened through No.12 mesh (710mm) to prepare small granules. The granules were dried at 50° C overnight in an oven and screened through a No.20 mesh.

Formulation No.3: Weighted 50g of paracetamol, 30.875g of lactose and 10.8125g of corn starch and dry-mixed using motor and pestle for about 5 minutes. The mixture was blended by tumbling for 10 minutes. The blended mixture was moistened by slowly addition of 10% gelatine solution to proper wetness and then kneaded well. The wet mass was screened through No.12 mesh (710mm) to prepare small granules. The granules were dried at 50° C overnight in an oven and screened through a No.20 mesh.

Preparation of Tablets: Weighted 2.25g of magnesium stearate, 6.75g of talc and 0.8125g of corn starch, mixed them together and screened the mixture through No.60 mesh. The mixture was then blended by tumbling with the granulation and the resulting mixture was compressed using hand tablet machine with punch diameter of 9mm. About 100 tablets were prepared for each formulation.

Table 1. Preparation of Paracetamol tablets with 9.2% binder (w/w)

	Formulation 1		Formulation 2		Formulation 3	
	Each Tablet (mg)	%	Each Tablet (mg)	%	Each Tablet (mg)	%
Paracetamol	100	40.7	100	40.7	100	40.7
Lactose	61.75	25.1	61.75	25.1	61.75	25.1
PVP	22.5	9.2	-	-	-	-
Starch paste	-	-	22.5	9.2	-	-
Gelatine solution	-	-	-	-	22.5	9.2
Mg stearate	4.5	1.8	4.5	1.8	4.5	1.8
Talc	13.5	5.5	13.5	5.5	13.5	5.5
Corn starch (dry)	43.25	17.6	43.25	17.6	43.25	17.6
Expected total wt. of a tablet	245.5		245.5		245.5	

Tests for Evaluation of Tablets

Weight uniformity test: Twenty tablets from each formulation were selected randomly and weighed individually using a highly sensitive electronic balance (Sartorius). Their mean weights were calculated. Using BP specifications for tablets, deviations and coefficients of variation for each batch were calculated.

Hardness test: Five tablets were selected at random from each formulation to perform this test. Tablet harness tester was used to measure the hardness. Tablet was placed between spindle and anvil of the tester and the calibrated length adjusted to zero. The knob was then screwed to apply a diametric compression force on the tablet and the position on the calibrated length at which the tablet broke was recorded in kgf units. A mean hardness was calculated for each batch and thus their standard deviations and coefficient of variations were calculated.

Friability test: Friabulator was used to carryout this test. Twenty tablets were selected at random, dusted and weighed together using the electronic balance (Sartorius) and then placed in the friabualtor. The machine was operated for 4 min at 25 rpm for 100 rotations. The tablets were carefully dedusted again and weighed. The percentage losses were calculated for each formulation of the tablets. Friability expressed as weight loss percentage. Test was repeated 3 times and the average was determined.

Disintegration time: The method specified in the USP/NF (1980) was used. The machine used was QC-21 Disintegration test system. Disintegration medium used was 100 ml water maintained at temperature between 35 and 39ºC throughout the experiment. Six tablets selected at random from each formulation were placed one in each of the cylindrical tubes of the basket and then placed the discs in each baskets. The time taken for each tablet to break up into small particles and pass out through the mesh was recorded. Mean disintegration time was calculated for each batch.

Dissolution test (Rotating basket method): SR8PLUS-Hanson Virtual Instrument, dissolution test station was used to carryout this test. Phosphate buffer (pH 6.8) was used as the dissolution medium. Dissolution test were performed for 2 tablets of each formulation. According to the procedure, 1 L of phosphate buffer (pH 6.8) was filled into each of the six beakers of dissolution apparatus. Two tablets from each formulation were taken and placed in small baskets made from a screen mash. The baskets were then immersed in dissolution medium and rotated at a given speed. Samples (5 ml) were removed at designated time intervals (t_0, t_{10}, t_{20}, t_{30}, t_{40}, t_{50} and t_{60}) and diluted 10 times and assayed for their paracetamol content spectrophotometrically at 243nm.

RESULTS AND DISCUSSION

Effects of binder on the uniformity of the weight (weight variation tolerance test) Results obtained are given in Table 2. According to the ingredients composition in Table 1, expected weight of the tablet would be 245.5mg. Experimental average weight of a tablet obtained for formulation 1, 2 & 3 are 253.5, 230.2 & 238.1 mg, respectively. According to the Table 2, it is clear that the all tablet samples complies from with the standard as the individual weight does not deviate from the mean (average value) more than permitted in terms of percentage (5% for tablet weight more than 250 mg and 7.5% for tablet weight more than 80mg and less than 250mg) as per the British Pharmacopoeia (BP). i.e. tablet weights measured for formulation 1, 2 & 3 were fallen into the following ranges, (253.5 ± 12.7), (230.2 ± 17.3) and (238.1 ± 17.9), respectively. The difference in average weights is due to the type and the concentration of binders. Average weight obtained for PVP is greater than the expected weight of 245.5mg (see Table 1). This is because PVP is a polymer binder produces viscous and tacky solutions [8]. PVP agglomerates the fine powder upon addition of alcohol as in the procedure and the tackiness aid to hold the individual granules together. So this strengthens the intergranular forces between granules as well as intragranular forces in each granule, resulting an increase in average weight. Average weights obtained for binders namely starch paste and gelatine solution, were less than the expected weight.

Table 2. Weight variation tolerance test result

Tablet number	Formulation 1		Formulation 2		Formulation 3	
	Each Tablet (mg)	% Deviation	Each Tablet (mg)	% Deviation	Each Tablet (mg)	% Deviation
1	256.0	1.1	237.0	3.0	235.0	-1.3
2	253.0	-0.1	242.0	5.1	234.0	-1.7
3	247.0	-2.4	220.0	-4.4	244.0	2.5
4	253.0	-0.1	229.0	-0.5	243.0	2.1
5	258.0	1.9	240.0	4.3	234.0	-1.7
6	256.0	1.1	229.0	-0.5	242.0	1.6
7	252.0	-0.5	234.0	1.7	231.0	-3.0
8	250.0	-1.2	223.0	-3.1	235.0	-1.3
9	255.0	0.7	240.0	4.3	239.0	0.4
10	256.0	1.1	234.0	1.7	245.0	2.9
11	254.0	0.3	222.0	-3.6	245.0	2.9
12	253.0	-0.1	220.0	-4.4	222.0	-6.8
13	253.0	-0.1	249.0	8.2*	225.0	-5.5
14	258.0	1.9	221.0	-4.0	238.0	0.0
15	243.0	-4.0	216.0	-6.2	243.0	2.1
16	254.0	0.3	225.0	-2.3	248.0	4.2
17	250.0	-1.2	231.0	0.3	234.0	-1.7
18	250.0	-1.2	237.0	3.0	233.0	-2.1
19	252.0	-0.5	231.0	0.3	242.0	1.6
20	260.0	2.7	223.0	-3.1	250.0	5.0
Average	253.2		230.2		238.1	

This indicates that the intergranular forces between granules in formulation 2 & 3 are fairly weaker than the desired strength.

However, gelatin solution as a binder excels the starch paste and gives average weight (238.1mg) close to the expected weight (see Table 1). When it compares the gelatin binder with PVP, gelatin binder again excels PVP as the PVP tablets are weighed. Increase in weight also increases the drug content of the tablet which is economically unacceptable. Another positive aspect of selecting tablet weight less than 250mg is the 7.5% weight variation according to BP which gives the manufacturing flexibility.

Effects of binder on the uniformity of the drug content

This test has not been carried out due to time constraints. But the uniformity of the weight observed above also indicates the probable uniformity in the drug content of the tablets. Tablets with gelatine binder would be the best in content of drug compared to others, as explained above.

Effects of binder on the tablet hardness and the tensile strength

Tablet hardness and calculated tensile strength were given in Table 3. It was observed that tablets hardness for all formulation was less than 4kg. This means that all tablets fail the hardness test may be due to experimental problems. However, it indicated that hardness varied with the binder type. Polymeric binder, PVP, and gelatin binder showed high values and starch binder gave the lowest value for hardness (see Table 3).

Tablet with gelatin solution also gave a fairly high value for hardness test. Hardness of tablets depends on the degree of binding which relies on the amount of the binder and the compression force. Higher hardness in tablet with PVP can be related to its film formation ability and its cohesive strength to make solid bonds between particles. Thus, it was reported that binders with plasto elastic properties undergo deformation under high compression pressure. As a result, binder is forced into the interparticulate spaces resulting more solid bond between granules [6]. This would be the reason to have higher hardness for tablet with gelatin binder. Starch paste lacks cohesiveness and shows very low hardness in tablets.

Table 3: Tablet hardness and tensile strength

Tablet No.	Formulation 1		Formulation 2		Formulation 3	
	Hardness (kg)	Tensile Strength	Hardness (kg)	Tensile Strength	Hardness (kg)	Tensile Strength
1	3.5	6.59	1.6	2.83	3.0	5.38
2	3.1	5.83	1.8	3.18	3.5	6.28
3	3.3	6.21	1.8	3.18	3.5	6.28
4	3.2	6.02	1.7	3.01	3.0	5.38
5	3.2	6.02	1.9	3.36	3.0	5.38
Average	3.26	6.13	1.76	3.11	3.2	5.74
Thickness(t)		0.38 cm		0.4 cm		0.39 cm
Diameter(D)		0.89 cm		0.9 cm		0.91 cm

Note: *Tensile strength (σt) was calculated by using the equation, $\sigma t = 2F/\pi Dt$.*

According to the Table. 3, it shows that the tablets with PVP and gelatine solution binders possess significantly higher tensile strength. Tensile strength is a measure for important mechanical properties of tablets, namely bond strength and lamination tendencies [9]. Higher tensile strength of tablets with PVP binder is a result of both film formation ability and the magnitude of the cohesive strength of the polymer binders [6]. Higher tensile strength of the tablets with gelatine solution can be related to its good spreading during the preparation of wet mass for granulation. The higher the spreading coefficient, is the stronger the tablet tensile strength [6]. Starch lacks in its cohesive strength and therefore gives very low tensile strength. This reveals that the properties of the binder itself are very crucial in evaluating tablet properties and making tablets with better quality.

Effects of binder on the friability

Friability corresponding to each binder, PVP, Starch paste and Gelatine solution, were 0.599%, 5.39% and 7.52% respectively. PVP tablet showed the lowest percentage weight loss indicating higher intergranular forces between the granules. So PVP is proved to be a good binder. The value obtained for gelatine solution binder is in question when it compare with the other evaluation parameters (3.1, 3.2 & 3.3). Therefore, it is considered as an experimental error.

Effects of binder on the disintegration time

Disintegration times obtained for three formulations were 13 min 52 sec, 6 min 28 sec and 8 min, respectively, and were compatible with the trend of the values obtained for average weight and hardness. Also they remain below 15 min. The intergranular bond strength decreases in the order of binders PVP > Gelatine Solution > Starch paste. The trend of disintegration times follows the similar trend as of other parameters, 3.1 & 3.3. So the values are technically and theoretically acceptable. Disintegration time is concerned, gelatine binder appear to be good for paracetamol tablet formulation.

Effects of binder on the dissolution rate

Calibration Curve: Calibration curve was prepared using standard solutions. Absorptions were measured at wavelength of 243 nm and plotted against concentrations. The equation for calibration curve with and without intercept was $y = 0.07x + 0.0454$ ($R^2 = 0.9956$) and $y = 0.0828x$ ($R^2 = 0.9864$), respectively. As the calibration curve should follow $y = mx$, the equation without intercept was used in paracetamol calculating concentrations at dissolution test (Table. 4).

As in the procedure, 5 ml samples taken at the different time interval were 10 times diluted. Taking this into consideration, concentrations were calculated using above equation. Concentration data were also plotted against the time and indicated in Fig. 1. The pH of the dissolution medium was maintained at pH 6.8 which is similar to pH in small intestine.

Table 4. Absorbance and calculated concentration obtained for dissolution test

Time (min)	Formulation 1		Formulation 2		Formulation 3	
	Absorbance	Concentration mg/L	Absorbance	Concentration mg/L	Absorbance	Concentration mg/L
T_0	0	0	0	0	0	0
T_{10}	0.058	7.0	0.424	51.2	0.361	43.6
T_{20}	0.0895	10.8	0.604	72.9	0.623	75.2
T_{30}	0.1625	19.6	0.654	79.0	0.984	118.8*
T_{40}	0.1775	21.4	0.658	79.5	0.1275	15.4
T_{50}	0.197	23.8	0.6635	80.1	0.1865	22.5
T_{60}	0.2045	24.7	0.6675	80.6	0.2165	26.1

**. Asteric mark under formulation 3 indicates an abnormal value obtained.*

Note: Concentrations were calculated using the calibration curve equation, y = 0.0828x

According to the Figure 1, it indicates that the tablets with PVP show very low dissolution performance. This observation is in agreement with the values obtained for hardness, friability and disintegration time when intergranular forces are concerned. The harder the tablet is the lower the dissolution performance. Tablets with starch paste binder exhibits fairly high dissolution rate in the first 20 minutes and then behave similar to the tablets of PVP binder. Tablets with gelatine solution as binder show complete dissolution in first 30 minutes. The sharp decrease after that can be correlated to the dilution takes place after every sample withdrawal with the addition of equal volume of buffer solution (dissolution medium of pH 6.8) in order to make the constant volume of dissolution medium in the beaker. However, these results are not in agreement with the 3.1, 3.3 and 3.5 above.

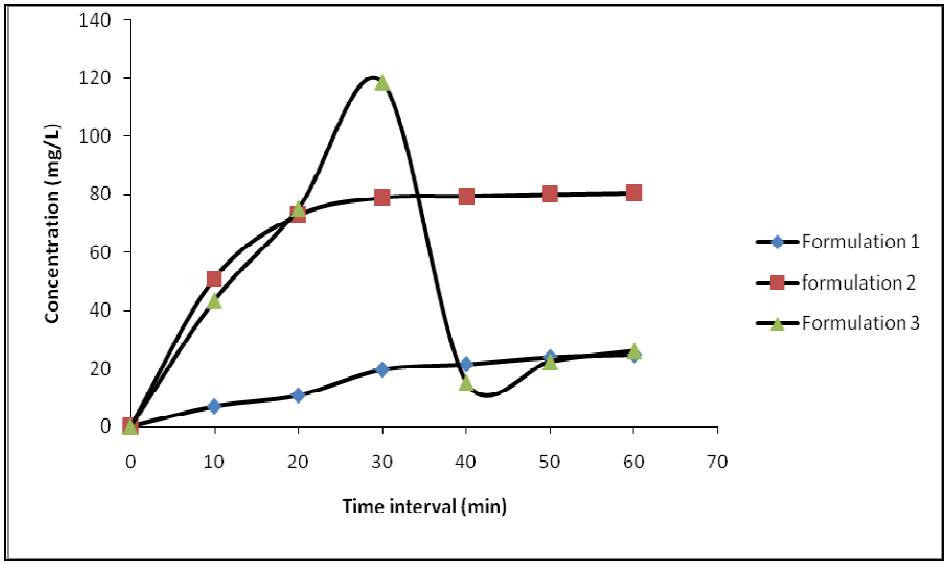

Figure 1 Dissolution profiles of formulation 1, 2 & 3 with the time

CONCLUSION

In conclusion, I would like to mention that the laboratory study on the effects of binder on the physico-chemical properties of the tablets has established the fact that the physic-chemical properties, type, quality and concentration of binder itself are key factors that affect the ultimate quality of the tablet. Results proved that the binders, PVP and gelatine solution, are good binders for preparation of paracetamol tablet but gelatine solution appeared to be better than the PVP binder. Starch binder is not suitable for making paracetamol tablets. Even though the variation of laboratory experimental results obtained for tablet evaluation parameters could be explained considering physic-chemical properties of binders, overall quality of the all tablets does not reach the standard required for good and quality tablets. This may be due to errors in the experimental conditions, e.g. method of addition of binder, mixing time etc. In order to do a complete evaluation of binder effect on the quality of tablets, it is proposed carry out following investigations for granules prepared related to powder flow properties such as angle of repose, flowability index, bulk and tapped densities, Carr's Index, Hausner ratio, particle size and size distribution, and moisture content after preparation of granules for each and every binder being tested. It was found that the strength of inter- and intra- granular forces entirely depend on the type of binder. They are the key forces that govern the all evaluation parameters. Therefore, choice of binder for formulation of powder dosage form is paramount important in preparing tablets with desired physic-chemical properties. To find the effects of binder on the physic-chemical properties of the binder, it is recommended to evaluate all parameters for at least three preparation of each formulation.

REFERENCES

[1] S. Mattsson, C. Nystrom, *Drug Dev. and Ind. Pharm.*, **2001,** 27(3), 181–194.
[2] S.K. Joneja, W.W. Harcum, G.W. Skinner, P.E. Barnum, Jian-Hwa Guo, *Drug Dev. and Ind. Pharm.*, **1999,** 25(10), 1129–1135.
[3] C. Nystrom, J. Mazur, J Sjogren, *Int. J. Pharmaceutics*., **1982,** 10, 209–218.
[4] M.D. Parker, P. York, R.C. Rowe, *Int. J. Pharmaceutics*., **1991,** 12, 243-249.
[5] M. D. Parker, P. York and R.C. Rowe, *Int. J. Pharmaceutics*., **1992,** 80, 179-190.
[6] R. C. Rowe, *Int. J. Pharmaceutics*, **1990,** 58, 209-213.
[7] I. Krycer, D.G. Pope, *Powder Technology*, **1983,** 34, 39- 51.
[8] B.M. Rahman, M.I.I. Wahed, P. Khondkar, M. Ahmed, R. Islam, R.K. Barman, M.A. Ul Islam, *Pak. J. Pharm. Sci*. **2008,** 21(4), 455-459.
[9] G. Alebiowu, O.A. Itiola, *Acta Pharm.*, **2003,** 53, 231-237.
[10] E.C. Ibezim, S.I. Ofoefule, E.O. Omeje, V.I. Onyishi, U.E. Odoh, *Scientific Research and Essay*, **2008,** 3(2), 46-50.
[11] Pharmaceutical Technology Report. American Association of Pharmaceutical Scientists Annual Meeting, Boston, MA **1997**.
[12] K. Zuurman, G.K. Bolhuis, H. Vromans, *Int. J. Pharmaceutics*. **1995**1, 19, 65-69.