EFFECT OF SURFACTANTS ON SOME PHYSICAL PROPERTIES OF PARACETAMOL TABLETS.

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Abstract

The effect of surfactants added to paracetamol (acetaminophen) granulations as well as the effect of the method of incorporating the surfactants on some physicochemical characteristics of the tablets have been investigated. Results obtained indicate that Tween® 80 treated granulation gave tablets with superior dissolution profile in comparison with tablets compressed from sodium lauryl sulphate treated granulation. This was inspite of the former having a longer disintegration time than the latter. Sodium lauryl sulphate when added extra granularly in the powdered from enhanced dissolution of paracetamol from the tablets more than when the surfactants was dissolved into the granulating liquid. Hardness of the paracetamol tablets was reduced in the presence of surfactants. Surfactants could be successfully used to enhance dissolution of poorly water soluble drugs such as paracetamol from solid dosage forms.

Introduction

Tablets are usually formulated with various excipients some of which are hydrophobic and may reduce dissolution of the active drug. A good tablet should be able to allow complete dissolution of the active drug over a short period of time, unless otherwise formulated. Since dissolution follows disintegration of tablets, earlier efforts to enhance the former concentrated on reducing the disintegration time. This was to a large extent achieved by the use of "super disintegrants" (1) However, accelerating disintegration may not significantly improve dissolution of active drug from a tablet. It has been conclusively demonstrated (2) that the particle size, and therefore the surface area into which a tablet disintegrates correlates with the dissolution rate.

In the recent past, surfactants have been added to tablet granulations in order to improve the wettability and dissolution of active drug from solid dosage forms (3 - 7). In developing and evaluating a pulsatile drug delivery system based on an impermeable capsule body filled with drug and an erodible plug placed in the opening of the capsule body, Krogel and Bodmeir (8) showed that erosion time of the compressed plugs decreased with the inclusion of surfactants. A study in which significant quantities of sodium lauryl sulphate were incorporated into an immediate release tablet formulation of a poorly water soluble immunosuppressive agent showed that the rate and extent of drug release was highly dependent on the mean particle size of the bulk drug (9).

This paper profiles a study in which surfactants are incorporated into paracetamol granulations in two different forms, and the physichochemical characteristics of the resulting tablets are compared.

Materials and Methods

Paracetamol powder (BP grade) was used as obtained from Neimeth Plc, Lagos, Nigeria. Maize starch BP, lactose and talc (BDH Chemicals, UK), magnesium stearate (Hopkin & Williams, UK), propyl paraben and methyl paraben (Gerhard Buchmann (KG - Tuttlingem, Germany), polyoxyethylene sorbitan monooleate - Tween ®80 and sodium laurly sulphate (Merck Damstadt, Germany) were used as received. All the sieves used were BSS sieves, water was double distilled, and every other chemical used was analytical reagent grade.

Preparation of granules

Paracetamol granules were prepared by the wet granulation method. Four batches of the granules were prepared in accordance with the formula listed in Table 1. Batch A contained sodium lauryl sulphate incorporated into the binder mucilage before granulation commenced. Batch B contained the same amount of sodium lauryl sulphate mixed intimately with the dry granulation before tabletting commenced. Batch C had Tween

® 80 incorporated into the binder mucilage as in Batch A. Batch D was prepared without surfactant.

Paracetamol and lactose were dry-mixed (Moulinex, France) for 10 min, and 5%w/v maize starch mucilage containing the appropriate amount of preservative as well as surfactant, where applicable, were added and wet-massed for 10 min. Enough quantity of mucilage was added until the formation of a damp mass which did not feel sticky when rolled with the fingers but rather formed a ball which broke easily when pressed lightly with the fingers. The wet granulation was forced through a 1.40 mm screen and dried in a hot air oven (Kottermann, Germany) at 50° C for 12 h. The dry mass was forced through a 1.18 mm screen and dried for a further 30 min. The granules were then mixed with the appropriate quantity of maize starch disintegrant, talc, magnesium stearate and surfactant where applicable.

Preparation of tablets

The die capacity of the single punch tablet press (Koln Niehl GmbH, Germany) fitted with 12.5 mm circular faced punches was adjusted to hold about 600 mg of granules (without surfactant). This capacity, as well as a constant pressure setting, were maintained throughout the compression of tablets.

After compression, the tablets were stored in a humidity chamber at 45 ± 5% relative humidity (RH) at ambient temperature for at least 2 days before being evaluated.

Evaluation of tablets

The individual weights of twenty tablets from each batch were measured (B 154, College Toldedo, Mettler, Switzerland). The friability (TA 3 R, Erweka Apparatebau GmbH, Germany) and hardness (Model 2E/205, Schleuniger, Switzerland) were determiend. The disintegration times of the tablets in water at 37 ± 0.5° C were determined in a BP test unit (MK IV, Manesty Machines, UK). The disintegration test unit was run for 15 min after which the medium was filtered through a 180 mm screen. The weight of the granules retained on the screen was determined. The mean of six such determinations was calculated as a percentage of the weight of the tablet.

Dissolution of paracetamol from the tablets was determiend in 0.1m HCl, pH 1.0, by the BP paddle method (ST 7, G.B. Caleva Ltd., UK). The drug content was spectrophotometrically determined (SP 1800, Pye Unicam, UK).

Results and Discussion

Some physical characteristics of the tablets are listed in Table 2. All the tablets met the BP requirements for tablet weight uniformity. The paracetamol tablets containing surfactants were softer than those without surfactant. This may have resulted from weakening of interparticulate bond strength in the compact. The tablets containing Tween® 80 were less friable than the others.

Sodium lauryl sulphate marginally shortened the disintegration time of the tablets. On the contrary, Tween ® 80 increased the disintegration time of the tablets. This result confirms an earlier report (10) that polysorbate 80 reduced the disintegrate efficiency of starch. The reduced tablet hardness as a result of the use of surfactants may be responsible for the ability of sodium lauryl sulphate to reduce the disintegration time of tablets (11).

The dissolution profiles of paracetamol from the various tablet formulations are shown in Figure 1. It is evident from the curves that the inclusion of surfactants into the granulations enhanced the dissolution of the active drug from the tablets. Dissolution was fastest from tablets containing Tween ® 80, followed by tablets containing sodium lauryl sulphate previously dissolved into the binder mucilage. Tablets without surfactant had the slowest dissolution of paracetamol. Within the first 5 min, the dissolution rates for tablets containing Tween ® 80, powdered sodium lauryl sulphate and dissolved sodium lauryl sulphate were 16.4% min 15.6% min and 14.9% respectively. Tablets without surfactant over the same period of time had a dissolution rate of 4.0min.

A detailed study of the size distribution of granules generated after disintegration of tablets containing surfactants led to the postulation that the action of surfactant in promoting drug dissolution from tablets containing it is likely to result from the ability of the surfactant

to influence the disintegration process rather than improving wettability per se 910). In this investigation, the amount of deaggregation, particles per tablet retained on a 0.180 mm screen after 15 min in the disintegration test equipment is used to quantify the degree of fragmentation which occurred during disintegration. Tablets without surfactant over the same period of time had a dissolution rate of 4.0% min.

A detailed study of the size distribution of granules generated after disintegration of tablets containing surfactants led to the postulation that the action of surfactant in promoting drug dissolution from tablets containing it is likely to result from the ability of the surfactant to influence the disintegration process rather than improving wettability per se (10). In this investigation, the amount of deaggreagted particles per tablet retained on a 0.180mm screen after 15 min in the disintegration test equipment is sued to quantify the degree of fragmentation which occurred during disintegration. Table 3 lists the amount of particles retained on the screen from each batch of paracetamol tablets after disintegration, as well as the amount of paracetamol dissolved after 10 and 30 min. The results show that the amount of retained particles decreased according to the rank order: Batch D > Batch A > Batch B > Batch C. The result is also an indication that Batch C disintegrated to produce the largest quantity of fines (<180mm) followed by Batch B, Batch A and Batch D, in that order. Based on the modified Noyes - Whitney equation, equation, ti would be expected that the more the amount of fine particles generated from tablet disintegration the larger would be the surface area available for dissolution; $dw/dt = kACs$.....i where w is the amount of drug that dissolves from a compact, k is the rate constant of dissolution per unit area, A is the surface are available for dissolution and Cs is the saturation solubility of the drug. The results of dissolution rate studies in this investigation are in accord with the equation.

The BP 1988 specified that at least 70% of the active drug content should dissolve from an uncoated tablet within 30 min. Based on this, it can be inferred that all the tablet formulations passed the BP dissolution rate test.

Conclusion

This investigation has established that various physicochemical parameters of compressed tablets are affected by surfactants. These parameters include friability, hardness and disintegration time. Dissolution of paracetamol from the tablets was positively affected by the surfactants. Tween R 80 was marginally superior to sodium lauryl sulphate in improving the dissolution profile from paracetamol tablets. The method of incorporating sodium lauryl sulphate also affects the physicochemical characteristics of the tablets.

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Table 1. Formula for preparing paracetamol granules.

Materials	Batch A	Batch B	Batch C	Batch D
Paracetamol	125g	125g	125g	125g
Maize starch disintegrant	7.5% w/v	7.5%w/v	7.5%w/v	7.5%w/v
Lactose	10g	10g	10g	10g
5%w/v maize starch mucilage	q.s.	q.s.	q.s.	q.s.
Propyl/methyl paraben	1%w/v	1%w/v	1%w/v	1%w/v
Talc	0.5%w/v	0.5%w/v	0.5%w/v	0.5%w/v
Magnesium stearate	0.5%w/v	0.5%w/v	0.5%w/v	0.5%w/v
Sodium lauryl sulphate	0.5%w/v	0.5%w/v	-	-
Tween®80	-	-	0.5%w/v	-

Table 2. Some physical characteristics of the paracetamol tablets

Batch	Weight of tablets (g)	Hardness (kp)	Friability (%)	Disintegration time (min.)
A	0.6162 (0.008)	6.58 (0.38)	4.1	0.95 (0.20)
B	0.6288 (0.011)	6.33 (0.26)	4.0	0.69 (0.24)
C	0.6590 (0.015)	6.80 (0.88)	3.3	5.24 (0.29)
D	0.6031 (0.012)	7.25 (0.52)	4.1	1.13 (0.10)

*Standard deviations are listed in parenthesis.

Table 3. Amount of deaggregated particles retained on a 0.180 mm screen after 15 min. in the disintegration test unit.

Batch	Residue retained on screen (%)	Amount dissolved (%) after 10min.	30min.
A	0.96	92.72	100.0
B	0.52	98.10	100.0
C	0.34	100.00	100.0
D	6.63	52.73	100.0

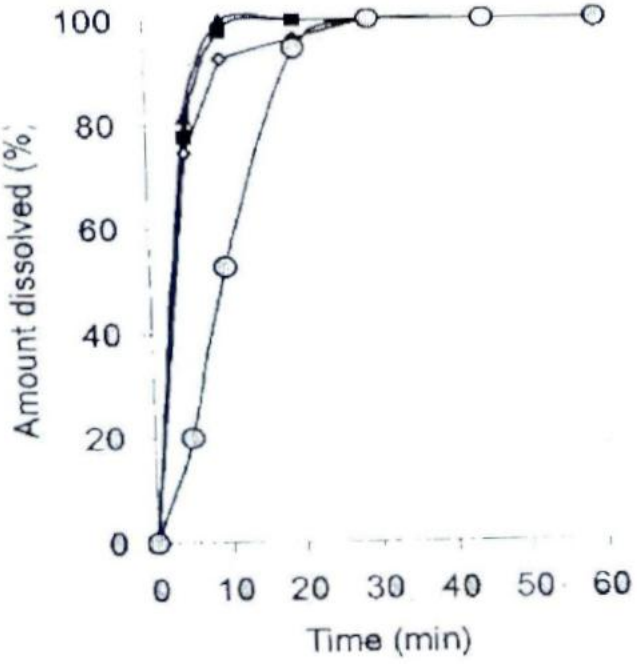

Figure 1. Effect of surfactant on dissolution of paracetamol from tablets.
Key: O without surfactant: ■ sodium lauryl sulphate used in the dry granulation; ◇ sodium lauryl sulphate used in the binder mucilage; △ with Tween®80.

REFERENCES

1. Shangraw, R., Mitrejev, A., Shah, M. (1980) A new era of tablet disintegrants. Pharm. Technol., 4, 49 - 57.
2. Rubinstein, M.A., Wells, J.I. (1977) Generated surface area measurement of disintegrating tablets. J. Phrm. Pharmacol. 29(6), 363 - 366.
3. Nasipuri, R.N., Omotosho, J.A. 91985) Influence of surfactant-treated starch on the disintegrant and dissolution of sulphadiazine tablets. J. Pharm. Pharmacol. 37(3), 212 - 213.
4. Singh, J. (1986) Effect of sodium lauryl sulphate and Tween® 80 on the therapeutic efficacy of glibenclamid tablet formulations in terms of BSL lowering in rabbits and diabetic human volunteers. Drug Dev. Ind. Pharm., 12(6), 851 - 866.
5. Singh, J., Jayaswal, S.B. (1986) Effect of surfactants on the permeation of lorazepam from its tablet formulations through rabbit jejenum sac. Pharmazie, 41(6), 435 - 436.
6. Wan, L.S.C., Heng, P.W.S. (1986) Action of surfactant on disintegration and dissolution of tablets containing microcrystalline cellulose. Pharm. Acta Helv., 61(5 - 6). 157 - 163
7. Wan, L.S.C., Heng, P.W.S. (1986) Influence of surfactant on the properties of granule and tablets containing sodium calcium alginate. Pharm. Acta Helv. 62(5 - 6), 169 - 174.
8. Krogel, I., Bodmeier, R. (1998) Pulsatile drug release from an insoluble capsule body controlled by an erodible plug. Pharm. Res. 15(3), 474 - 481.
9. Ruddy, S.B., Matuszewska, B.K., Grim, Y.A., Ostovic, D., Storey, D.E. (1999) Design and characterization of a surfactant enriched tablet formulation for oral delivery of a poorly water-soluble immunosuppressive agent. Int. J. Pharm., 182(2), 173 - 186.
10. Heng W.S., Wan L.S.C., Ang T S.H. (1990) Role of surfactant on drug release from tablets. Drug Dev. Ind. Pharm. 16(6), 950 - 962.
11. Ingram, J.T., Lowenthal, W. (1972) Mechanism of action of starch as a tablet disintegrant. II Effects of pepsin and surfactants on swelling of starch grains at 370 C. J. Pharm. Sci. 57, 187 - 188.