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RESEARCH ARTICLE

Effect of Lubricants on Flow Properties and Tablet Strength of Silicified Microcrystalline Cellulose

M. A ODENIYI*°, J. ALFA**, K. T. JAIYEOBA*

Effect of Lubricants on The Flow Properties and Tablet Strength of Silicified Microcrystalline Cellulose

Summary

The effects of magnesium stearate, sodium lauryl sulphate (SLS) and talc as lubricants on some powder and tablet properties of silicified microcrystalline cellulose (SMCC) were studied. Single and binary blends of talc, magnesium stearate and SLS at 1% concentration were evaluated as flow modulators on SMCC. Influence of the lubricants on the powder and tablet properties of metronidazole was also investigated. A similar grade of regular microcrystalline Cellulose (MCC) was used as control. The bulk and tapped densities, Hausner factor (Hf), and angle of repose (θ) were the basis for evaluation of the powders. Compacts of the powder blends were made at fixed compression force of 25 KN and evaluated on the basis of crushing strength.

Magnesium stearate, SLS or talc did not have an adverse impact on the powder fluidity and crushing strength of SMCC except that loss of crushing strength of about 20% was recorded in the batch containing 1% w/w magnesium stearate. The binary blends of talc + SLS or talc + magnesium stearate enhanced the fluidity of MCC as Hf was reduced to 1.2 while θ was below 24° compared to 33.9° in the control. The results indicate that SMCC possesses some inherent lubricating properties. However, in tabletting a highly cohesive drug, a limited concentration of an external lubricant may be useful.

Key Words: *Lubricants, compression, flow, microcrystalline cellulose, silicified microcrystalline cellulose.*

Silislenmiş Mikrokristalize Selülozun Akış Özellikleri ve Tablet Direnci Üzerine Lubrikanların Etkisi

Özet

Lubrikan olarak kullanılan magnezyum stearat, sodyum lauril sülfat (SLS) ve talkın silislenmiş mikrokristalize selülozun (SMKS) toz ve tablet özellikleri üzerine etkileri incelenmiştir. SMKS'nin akışı üzerine tekli veya ikili karışım halinde %1 konsantrasyonda talk, magnezyum stearat ve SLS'ın etkisi değerlendirilmiştir. Ayrıca lubrikanların metronidazolün toz ve tablet özellikleri üzerine etkileri de incelenmiştir. Benzer kalitedeki normal mikrokristalize selüloz (MKS) ise kontrol amacıyla kullanılmıştır. Toz ve vuruş dansiteleri, Hausner faktörü (Hf) ve yığın açısı tozların değerlendirilmesinde esas alınmıştır. Toz karışımlarının sıkıştırılması 25 KN'luk sabit basım kuvveti uygulanarak gerçekleştirilmiş ve kırılma direnci yönüyle değerlendirilmiştir.

Magnezyum stearat, SLS veya talk toz akışkanlığı ve SMKS'un kırılma direnci üzerine herhangi bir olumsuz etkisi görülmezken, %1 (a/a) magnezyum stearat içeren seride ise kırılma direncinde yaklaşık % 20'lik azalma gözlenmiştir. Talk + SLS veya talk + magnezyum stearat ikili karışımları ile MKS'un θ değeri 24° nin altında (kontrol grubu 33,9°) kaydedildiğinde H_f değeri 1,2'ye düşmüş ve tozun akışkanlığı artmıştır. Sonuçlar SMKS'un kendisinin lubrikan özelliğe sahip olduğunu göstermektedir. Bununla birlikte yüksek kohesif özellikteki ilaçlar tablet haline getirilirken kısıtlı miktarda lubrikanın dışarıdan ilave edilmesinde yarar olacaktır.

Anahtar kelimeler: *Lubrikanlar, basım, akış, mikrokristalize selüloz, silislenmiş mikrokristalize selüloz*

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INTRODUCTION

Direct compression is the preferred manufacturing process for pharmaceutical tablets, according to the survey conducted by Shangraw and Demarest (1), this may be due to the basic two-step process comprised of mixing and compressing (2). It is, however, important that while awareness is established on the production speed and cost, there is still no compromise on the quality of the resulting product. Selection of suitable excipients is one of the crucial steps that could mar or make a success in direct compression processing. A good number of direct compression excipients abound commercially and the dexterity of the formulator in

* Dept of Pharmaceutics & Industrial Pharmacy, University of Ibadan, Nigeria.
** Pharmaceutical Services Division, National Assembly Complex, Arms Zone, Abuja, Nigeria
° Corresponding author E-mail: deleodeniyi@yahoo.com

their selection determines the quality of the resulting product. The development and exploration of microcrystalline cellulose (MCC) in the early sixties as a tablet excipient brought a dramatic turn in direct compression phenomenon. It was classed as the single most important compression excipients (3), mainly due to excellent compressibility. More recently, a patented co-processing technology that involves a combination of colloidal silicon dioxide with MCC has been used to produce silicified microcrystalline cellulose (SMCC). SMCC products offer high synergistic flow and compaction qualities compared to the conventional MCC grades. SMCC also shows greater bulk densities than regular MCC, which can be explained by the improved flowability and packing properties due to the presence of silicon on the excipient (4).

Drugs, which have poor fluidity and compressibility potentials, require incorporation of appropriate adjuncts that would ensure desirable formulation characteristics. Although the sterling qualities of SMCC have been reported, it is important that the practicability of its use without compromising optimal formulation and bioavailability qualities of a therapeutic agent is investigated. Glidants and lubricants are often added to tablet formulations in order to modulate the fluidity and prevent the dosage form from sticking to the processing machinery. The alkaline stearates, particularly magnesium stearate and micronised silicas such as cab-o-sil and syloid have been employed as lubricant or glidant in formulations involving the use of MCC as filler – binder.

A previous study (5) showed the superiority of SMCC to MCC in terms of both flow and tablet properties in a formulation containing metronidazole, a drug with poor compressibility and fluidity profiles (6). However, the mechanical strength of a pharmaceutical tablet is not only determined by its active formulation components, but is also affected by lubrication (7). A good excipient should have low lubricant sensitivity, and should not adversely affect formulation properties (8,9). Hence the effect of different lubricants was evaluated on the flow and mechanical properties of direct compressed metronidazole tablet formulations containing SMCC using MCC as control.

MATERIALS AND METHODS

Prosolv™ HD 90, Emcocel® 90 (Penwest, Patterson, N.Y): Metronidazole (Vision Pharmaceutical Co. Ltd. China): Talc (Sigma-Aldrich Co. Ltd, Gillingham-Dorset, UK): Magnesium stearate (M & B London UK): Sodium lauryl sulphate (Fisons Plc, Loughborough, UK) were used as obtained from the suppliers.

Blending of powders: Batches of SMCC or MCC formulations were made so as to contain 0, 0.25, 0.50, or 1.0% of SLS or magnesium stearate while those made with the glidant contained talc at 1, 1.5, and 2.0%. In each case, appropriate quantities of the excipients sufficient to produce 50 compacts of 500 mg each were blended for 5 minutes using a small scale planetary mixer.

To study the influence of drug on the flow properties of the excipients, 10–30% of SMCC or MCC were added and blended with metronidazole.

Measurement of powder flow properties: The bulk density (β_p) and tapped density (β_T) of powders were determined using the Stamfvolumeter Model STAV (JEF Germany). A 50 g weight of the sample was placed inside the graduated cylinder and tapped for 500 times. Volumes of powder before and after each tapping were recorded. Hausner factor was derived as $\beta_T / \beta_{p.}$ The angles of repose were calculated using the expression: $\tan \theta = 2h/D$ where h and D respectively are the measured height and diameter of the cone formed by the poured powder. In addition, the flow rate of the powder was determined as the ratio of mass (g) to time (seconds); a steel funnel (orifice: 10, 15, and 25 mm diameter; DIN 53916) was used.

Compression: 500 mg blends of SMCC or MCC with talc, magnesium stearate or SLS were compressed at a fixed force of 22.5 KN using a basket type tablet machine Model THP (STC Pharmaceutical Machinery Co. Ltd, China) fitted with a punch of 12 mm diameter. The crushing strength of the resulting compacts was determined using the Erweka hardness tester Model DT (Erweka GMBH Germany). Three different determinations were made and the average was taken as the crushing strength of the batch.

STATISTICAL ANALYSIS

The Student's unpaired t-test was applied to the results obtained at 95% confidence interval, 2-tailed *p* values less than or equal to 0.05 were considered significant.

RESULTS AND DISCUSSION

The effects of lubricants on the flow properties of SMCC and MCC are shown in Tables 1–3. Addition of magnesium stearate or sodium lauryl sulphate did not significantly ($P > 0.05$) affect the angle of repose of SMCC. As a general guide, powders with angles of repose greater than 50° have unsatisfactory flow properties; above 40° flows are irregular, whereas, angles close to 25° are suggestive of good flow properties (10). The angles of repose (θ) and H_f of the direct compression excipients were within such ranges as could be classed as good flow behaviour. Thus, the added lubricants did not adversely affect the fluidity of SMCC.

Compact strength was not adversely affected in SMCC compared to MCC, where loss of strength in the range of about 25 to 50% was noticed in batches containing magnesium stearate (Figure 1). This is similar to an earlier finding that hydrophobic lubricants such as magnesium stearate could cause an appreciable loss in the strength of MCC compacts at lubricant concentration above 0.5% (2). At higher lubricant concentration, the enlarged contact surfaces

Table 1. Characterization of radicals detected by ESR techniques.

Magnesium stearate (%w/w)	Angle of repose (θ)		Hausner factor (H_f)		Hardness (KgF)	
	SMCC	MCC	SMCC	MCC	SMCC	MCC
0	15.4	33.9	1.2	1.3	5.5	4
0.25	22.6	26.8	1.2	1.3	4.5	3.0
0.50	25.0	25.7	1.2	1.2	4.0	2.0
1.0	22.8	25.5	1.2	1.3	3.5	2.0

Table 2. Effect of Sodium Lauryl Sulphate on the flow and tablet properties of Silicified microcrystalline cellulose (SMCC) and Microcrystalline cellulose (MCC)

Sodium lauryl sulphate (% w/w)	Angle of repose (θ)		Hausner factor (Hf)		Hardness (KgF)	
	SMCC	MCC	SMCC	MCC	SMCC	MCC
0.00	15.4	33.9	1.2	1.3	5.5	4
0.25	23.3	26.2	1.2	1.3	4.5	4.2
0.50	21.3	27.0	1.2	1.3	4.5	3.2
1.00	22.7	25.5	1.2	1.3	4.5	3.5

Table 3. Effect of talc on the flow and tablet properties of Silicified microcrystalline cellulose (SMCC) and Microcrystalline cellulose (MCC)

Talc (% w/w)	Angle of repose (θ)		Hausner factor (Hf)		Hardness (KgF)	
	SMCC	MCC	SMCC	MCC	SMCC	MCC
0.00	15.4	33.9	1.2	1.3	5.5	4.0
1.00	22.6	25.8	1.2	1.3	5.0	4.0
1.50	22.4	26.7	1.2	1.3	4.5	4.0
2.00	22.8	28.6	1.2	1.3	4.5	4.0

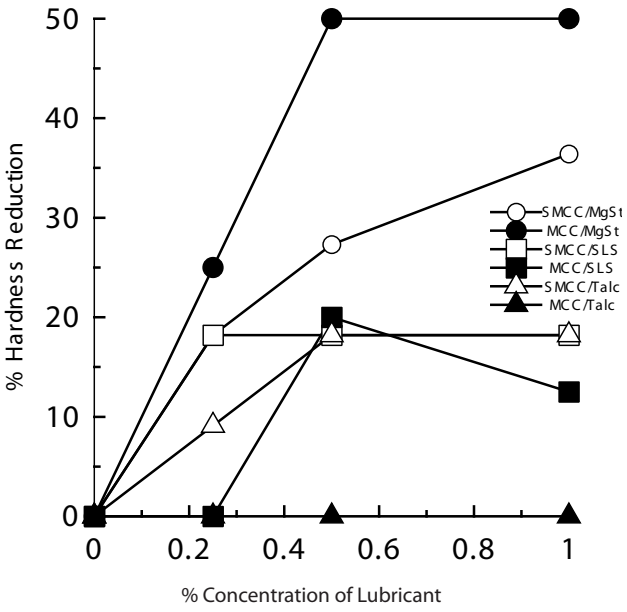

Figure 1. Influence of lubricants of the hardness reduction of SMCC and MCC compacts

Key:
SMCC/MgSt: silicified microcrystalline cellulose/Magnesium Stearate blend; MCC/MgSt: microcrystalline cellulose/ Magnesium Stearate blend; SMCC/SLS silicified microcrystalline cellulose/Sodium laurylsulphate blend; MCC/SLS: microcrystalline cellulose/Sodium laurylsulphate blend; SMCC/ Talc: silicified microcrystalline cellulose/talc blend; MCC/Talc: microcrystalline cellulose/talc blend

created during plastic deformation are covered by the alkaline stearate lubricant film, which acts as a physical barrier (11), thereby limiting the sites for bonding and consequently lowered compact strength. The extent of compact strength lowering by SLS is not as significant as produced by magnesium stearate, as only a loss of 20% in compact strength was observed. Magnesium stearate is superior to SLS as lubricant and less coverage of the possible binding sites might be responsible for the higher compact strength in formulations containing SLS. Figure 1 also shows a slight reduction in the strength of SMCC compact when lubricated with talc. On the other hand, MCC/ talc blends did not exhibit lowered compact strength. The impression is that SLS might be employed as lubricant to complement the inherent lubricating activity of MCC in some formulations, providing that the surface acting property of SLS does not compromise with pharmaceutical or bioavailability properties of the drug. This result could be explored in direct compression formulation of drugs where MCC is employed. The slight lubricating effect of talc coupled with its crystalline nature might have constituted some advantage over magnesium stearate and SLS during the compression of the MCC.

The effect of binary blends of talc and SLS or magnesium stearate was investigated and the results are presented in Table 4. Interestingly, the angles of repose (θ) were significantly lowered by the blends of lubricants compared to those of the batches containing either of the excipients. The Hausner factor was also reduced to 1.2, which is an indication of good flow tendency. The blends of these lubricant materials most likely exhibited some synergistic effect in reducing the interparticulate frictional force between the fluffy particles of the microcrystalline cellulose resulting in lowered powder porosity, increased bed density and good powder flow.

Adequate flow propensity is a crucial factor in the selection of excipient for direct compression tabletting process. Formulations which exhibit good flow characteristics have potentials of ensuring short production time and uniform drug content, which are some of the desirable qualities in tabletting. The packing and flow characteristics of the formulations were determined and the results are presented in Table 5. The Hausner factor (H_f) and flow rates (FR)

Table 4. Effect of binary blend of lubricants on the flow properties of microcrystalline cellulose (MCC)

Talc	MgSt	SLS	Angle of Repose (θ)	Hausner factor (Hf)
–	-	-	33.9	1.4
0.25	0.75	-	23.4	1.1
0.50	0.50	-	22.4	1.2
0.75	0.25	-	23.9	1.2
0.25	–	0.75	23.4	1.2
0.50	–	0.50	23.4	1.2
0.75	–	0.25	23.4	1.2
1.00	–	-	25.8	1.3
-	1.00	-	25.5	1.3
-	–	1.00	25.5	1.3

MgSt = magnesium stearate, SLS = sodium lauryl sulphate

Table 5. Physical properties of metronidazole –excipient powder mix.

Excipient	(% w /w)	Poured bulk density (bp) (g/ml)	Tapped bulk density (bT) (g/ml)	Hausner ratio (Hf)	Flow Rate (g/s)
Nil	-	0.56	0.76	1.4	-
MCC	30	0.54	0.71	1.3	8.9
SMCC	17	0.60	0.78	1.3	10.0
SMCC	20	0.60	0.78	1.3	10.0
SMCC	25	0.65	0.80	1.2	14.8

values show that incorporation of SMCC imparted superior flow quality to the metronidazole powder when compared with corresponding grade of MCC. The better flow characteristic could be due to a higher degree and uniformity of coverage of the drug surface by the excipient, which led to a higher adhesion force reduction between the particles (12).

CONCLUSION

The study confirms that SMCC possesses some inherent lubricating qualities, and thereby is superior to MCC. However, in tabletting a highly cohesive drug, a limited concentration of an external lubricant may be useful.

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