*Bull. Pharm. Sci., Assiut University*
*Vol. 7, Part 1, pp. 1-14*

# EFFECT OF VARIOUS VEHICLES ON THE UNIFORMITY OF DRUG CONTENTS OF DIRECTLY COMPRESSED CHLORAMPHENICOL TABLETS

A.E. Aboutaleb & S.E.Saleh

Department of Industrial Pharmacy, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

## ABSTRACT

*Chloramphenicol tablets were prepared using various concentrations of directly compressible vehicles. It was found that Avicel and STA-R produced suitable chloramphenicol tablets which comply with B.P. requirements. On the other hand Sugartab, Anhydrous lactose, Emcompress and Celutab gave rise to tablets with long disintegration time. It was found also that all the batches were uniform with regard to their drug contents except for those tablets containing different concentrations of Sugartab. This may be due the difference in the physical properties between chloramphenicol and Sugartab powders.*

## INTRODUCTION

The direct compression techinque offers several advantages over the traditional granulation methods. These include, reduced cost, improved product stability and increased product reliablity[1].

It was stated[2] that no single material has been found that is suitable for all direct compression formules, so comparative study of directly compressible excipients with the medicaments is very important to establish the most

convenient vehicle.

In this report directly compressed chloramphenicol tablets were prepared using different concentrations of the various single vehicles, these tablets were evaluated with regard to their physical standards and uniformity of drug contents in order to evaluate the direct compression as a technique for preparing chloramphenicol tablets.

## EXPERIMENTAL

### Materials:

Microcrystalline cellulose (Avicel PH 101)[a], directly compressible starch marketed as STA-$R_x$1500[b], dicalcium phosphate dihydrate marketed as Emcompress special[c], Sugartab (processed sucrose)[c], lactose U.S.P. Anhydrous[d], Spray crystallized maltose dextrose marketed as Celutab[c], Chloramphenicol[e], magnesium stearate[f] and stearic acid[f],

### Equipment:

Manesty $F_3$ single punch Eccentric tablet machine[g], Erweka hardness tester[h], Roche friabilator[i], B.P. disintegration apparatus[i], Micrometer[j], set of sieves and vibrating shaker[k].

---

a- FMC Corporation, Pensylvania, U.S.A.
b- A.E.Staley, MFg Co., Decature, Illinois, U.S.A.
c- Edward Mendell Co. Inc., New York, U.S.A.
d- Shiffield Chemical Union, N.L. 07083, U.S.A.
e- El-Nasr Chemical & Pharmaceutical Company, Cairo, Egypt
f- CID Co., Assiut, Egypt.
g- Manesty Machines Ltd., Liverpool England.
h- Erweka-Apparateau, Frankfort, Western Germany.
i- City Laboratory, Cairo, Egypt.
j- Baty Dial Micrometer Model 120-1206, Baty & Co., Ltd, Sussex, England.
k- Laboratory, type ILM, Metall weberi Neustant-orala. Western Germany.

**Procedures:**

A) **Physical characteristics of the powders used:**

The particle size, bulk density and the flow property (angle of repose) were determined for the six excipients used and chloramphenicol powder using the method reported[3].

B) **Tableting:**

Chloramphenicol powder was used as received from the manufacturer, the tablets were prepared by mixing it with certain amount of the tested vehicle and lubricant. The following concentrations of single vehicles were used for the preparation of chloramphenicol tablets, 0, 19.61, 32.68, 42 and 49% w/w. Mixing was carried out in a drum mixer for a period of 15 minutes. The manesty, $F_3$ single punch eccentric tablet compression machine was set to produce tablets which were flat, scored, 6.4 $\pm$ 0.01 mm in diameter and have an average weight of about 0.1g. The machine was adjusted first for the compression of the tablets containing 49% w/w of the tested vehicles and then the adjustment was kept constant to compress the other concentrations of the same vehicle A minimum of 1000 tablets were produced for each batch.

Evaluation of tablets:

a) **Physical standards:**

All the manufactured tablets were evaluated for uniformity of weight (B.P. 1973), uniformity of thickness, hardness (Erweka), friability (Roche), and disintegration time (Modified B.P. 1968), according to the previously published procedures[4]:

b) **Uniformity of drug contents:**

Ten tablets from each batch were individually assayed for its chloramphenicol content . The absorbance was read at 278 nm in 0.1 N hydrochloric acid, the mean drug content, the standard deviation and C.V.% are given in Tablets 3-7.

## RESULTS AND DISCUSSION

Data in table (1) show that the flow rate represented by the angle of repose takes the following sequence: STA-$R_x$ 1500 > Celutab > Emcompress > Sugartab > Anhydrous lactose= Avicel > Chloramphenicol. So chloramphenicol powder is very poor with regard to its flow property and this may be the cause of difficulty in compressing it directly. From this Table it can be noticed also that the average particle size takes the following manner: Sugartab > Chloramphenicol > Celutab > Emcompress > Anhydrous lactose > STA-$R_x$ 1500 Avicel. It is clear that the flowability is not dependent only on the particle size of the material. Similar findings were obtaind by other workers[3]. Table(1) shows also the similarity and dissimilarity among the powders under test, which will be reflected on the physical characteristics of the produced tablets.

### Uniformity of weight and thickness:

Chloramphenicol alone cannot be compressed directly because of its bad flow property as well as small bulk density as shown in Table 1. The physical characteristics of the batches produced using various concentrations of the single vehicles are given in Table 2. From this Table, it is clear that all these batches passed the B.P. 1973 test for uniformity of weight, except for those which are marked by a star in the Table. The batches which failed to pass the test are those which were prepared using relatively small concentrations (19.61%) of the direct compression vehicles, and this is logical as chloramphenicol alone is non-compressible. The

increase in the proportion of the direct compression vehicle will therfore improve the flow property of the mixture as well as its compressiblity. Consequently the uniformity of weight will be increased by increasing the proportion of the vehicle[5].

The uniformity of thickness was found to go side by side with the uniformity of weight as shown in Table 2. Furthermore, the uniformity of thickness as indicated by the percentages coefficient of variation was also improved as the proportion of the vehicle increased in the formula.

**Disintegration time:**

Chloramphenicol tablets prepared using Avicel passed the B.P. 1973 test for disintegration as shown in Table 2. The other tested vehicles produced tablets with longer disintegration times, which were found to decrease by increasing the proportion of the vehicle in the formula.

**Hardness:**

From the data given in Table 2. It can be seen that the hardness increased as the concnetration of the vehicle increased in the formula. This is logical as the compressibility and consequently the mechanical property will be improved.

**Friability:**

The friability was found to decrease by increasing the concentration of the vehicle in the formula as shown in Table 2. The tablets prepared using 19.6% concentration of the different vehicles were found to be friable, with loss% =1.5, this was also the case on using Celutab at different concentrations. The later case may be due to the capping tendency which was noticed especially at 19.6%

concentration.

**Uniformity of drug contents:**

Table 3 shows the drug contents of chloramphenicol tablets containing 19% w/w of the various vehicles. It was found that all batches were uniform except those containing Celutab. This may be due to the difference in the packed bulk density as well as angle of repose between chloramphenicol powder and Celutab which led to improper and non-uniform filling of the die of the tablet press.

Table 4 shows the uniformity of contents of chloramphenicol tablets containing 32% w/w of the various vehicles. It was found that all batches comply with requirement of B.P. 1973 (variation did not exceed ± 10% w/w) except for those batches containing STA-$R_x$ and Sugartab. This may be due to large difference in particle size between both STA-$R_x$, Sugartab and Chloramphenicol; STA-$R_x$ has nearly 1/3 the average particle size of chloramphenicol while Sugartab has nearly double the average particle size of chloramphenicol. This large difference in particle size between the drug and the vehicles may lead to segregation and therefore improper filling of the die. The difference in the angle of repose between the various ingredients may also account for the non-uniformity of drug contents of the batches containing STA-$R_x$ as well as Sugartab[6].

Table 5. shows the drug contents of chloramphenicol tablets containing 42% w/w of the various vehicles. It was found that all batches comply with B.P. requirement except for those containing Sugartab which may be due to the difference in particle size[7]. The increase in the proportion of the vehicle to 49 w/w improved the uniformity of drug contents especially for those batches containing STA-$R_x$ as shown in

Table 6 except for those batches containing Sugartab. It is of interest to notice that the increase in the proportion of vehicle not only improved the physical standards of the produced tablets as mentioned previously but also gave rise to tablets with uniform drug content, except in the case of Sugartab which was found to be unsuitable at all concentrations used as it gave rise to non-uniform tablets. The effect of various concentrations of the different vehicles on the uniformity of drug contents of chloramphenicol tablets was shown in Table 7.

Table 1: The physical properties of chloramphenicol powder and the directly compressible vehicles used.

| *Material* | *Average particle size (u)* | *Packed bulk density* | *Angle of repose* |
|---|---|---|---|
| Chloramphenicol | 399.47 | 0.3268 | $51^{\circ}$ .20 |
| Avicel | 82.99 | 0.3546 | $40^{\circ}$ .00 |
| STA-$R_x$1500 | 113.21 | 0.6684 | $28^{\circ}$ .30 |
| Celutab | 342.58 | 0.6831 | $31^{\circ}$ .58 |
| Anhydrous lactose | 185.07 | 0.5593 | $40^{\circ}$ .00 |
| Sugartab | 661.12 | 0.6410 | $36^{\circ}$ .42 |
| Emcompress | 194.61 | 0.9025 | $35^{\circ}$ .36 |

**Table 2: Effect of single vehicles on the physical characteristics of chloramphenicol tablets**

| Vehicles | | Weight (gm) | | Thickness (mm) | | Hardness (Kg) | | Friability (Loss.%) | | D.T. | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Name | Conc.% w/w | mean | C.V.% | mean | C.V.% | mean | C.V.% | mean | C.V.% | Mean | C.V.% |
| Avicel | 19.6* | 0.0935 | 7.81 | 2.81 | 0.37 | 0.60 | 29.13 | 7.56 | 20.35 | 0.44 | 41.42 |
| | 32.6 | 0.1069 | 2.62 | 2.86 | 0.39 | 1.85 | 22.25 | 1.45 | 8.57 | 1.00 | 55.35 |
| | 42 | 0.1031 | 1.55 | 2.88 | 0.27 | 1.98 | 35.02 | 1.33 | 8.57 | 0.36 | 23.99 |
| | 49 | 0.1121 | 1.61 | 2.93 | 0.24 | 3.70 | 15.54 | 0.70 | 2.74 | 2.26 | 51.54 |
| Anhydrous lactose | 19.6* | 0.0878 | 7.18 | 2.63 | 0.86 | 0.50 | 0.09 | 7.65 | 3.81 | 99.80 | 7.83 |
| | 32.6 | 0.1122 | 4.55 | 2.74 | 1.76 | 2.98 | 31.38 | 3.73 | 5.81 | 118.00 | 29.73 |
| | 42. | 0.1178 | 0.93 | 2.85 | 0.38 | 4.35 | 13.87 | 1.22 | 2.32 | 120.00 | ----- |
| | 49 | 0.1244 | 1.05 | 2.94 | 0.80 | 6.10 | 16.22 | 0.80 | 9.57 | 94.60 | 6.84 |
| STA-$R_x$ | 19.6 | — | — | -- | — | --- | -- | -- | --- | --- | --- |
| | 32.6* | 0.0787 | 8.39 | 2.30 | 1.83 | 1.33 | 43.62 | 5.14 | 9.86 | 0.19 | 8.54 |
| | 42 | 0.0955 | 9.42 | 2.44 | 2.35 | 2.68 | 34.59 | 1.26 | 1.83 | 0.37 | 27.01 |
| | 49 | 0.1140 | 2.28 | 2.80 | 2.32 | 5.20 | 17.03 | 0.55 | 9.12 | 0.74 | 13.30 |
| Sugartab | 19.6 | -- | -- | -- | -- | -- | -- | -- | --- | --- | --- |
| | 32.6* | 0.1178 | 2.04 | 2.65 | 1.25 | 3.00 | 19.07 | 2.09 | 2.80 | 125.30 | 7.84 |
| | 42 | 0.1204 | 2.82 | 2.68 | 1.68 | 3.30 | 17.77 | 1.44 | 1.80 | 61.70 | 8.71 |
| | 49 | 0.1311 | 2.44 | 2.88 | 2.28 | 3.90 | 22.25 | 1.55 | 0.01 | 65.80 | 7.12 |
| Emcompress | 19.6* | 0.0814 | 7.13 | 2.23 | 0.54 | 1.30 | 31.14 | 4.38 | 13.87 | 120.00 | ——— |
| | 32.6 | 0.1209 | 1.24 | 2.47 | 0.54 | 3.78 | 25.45 | 1.40 | 8.78 | 120.00 | ——— |
| | 42 | 0.1394 | 1.51 | 2.71 | 0.84 | 5.55 | 20.12 | 2.77 | 7.63 | 120.00 | ——— |
| | 49 | 0.1531 | 0.78 | 2.90 | 0.50 | 7.35 | 12.65 | 2.24 | 2.57 | 120.00 | ——— |
| Celutab | 19.6* | 0.0910 | 8.68 | 2.20 | 4.55 | 1.68 | 26.37 | 11.17 | 24.06 | 120 | ——— |
| | 32.6 | 0.1072 | 3.45 | 2.38 | 3.44 | 3.23 | 14.82 | 4.82 | 3.76 | 126.70 | 5.34 |
| | 42 | 0.1266 | 2.13 | 2.83 | 2.25 | 4.58 | 22.76 | 2.45 | 0.26 | 114.80 | 10.63 |
| | 49. | 0.1524 | 0.98 | 3.46 | 1.10 | 6.10 | 16.53 | 2.26 | 2.77 | 116.00 | 6.14 |

Table 3: Drug content of chloramphenicol tablets containing 19% w/w of the various vehicles

| | *Avicel* | *Anhydrous lactose* | *STA-$R_x$* | *Sugartab* | *Encompress* | *Celutab* |
|---|---|---|---|---|---|---|
| Mean | 107.10 | 1[illegible] | Non-Compressible | Non-Compressible | 105.[illegible] | [illegible].08 |
| S.D | 5.14 | 4.89 | -- | -- | 3.19 | 8.03 |
| C.V. | 4.80 | 4.74 | -- | -- | 2.97 | 8.10 |

Table 4: Drug content of chloramphenicol tablets containing 32% w/w of the various vehicles

| | *Avicel* | *Anhydrous lactose* | *STA-R$_x$* | *Sugartab* | *Emcompress* | *Celutab* |
|---|---|---|---|---|---|---|
| Mean | 96.39 | 92.45 | 111.82 | 88.08 | 92.71 | 93.55 |
| S.D. | 1.46 | 5.95 | 2.58 | 5.36 | 7.78 | 3.25 |
| C.V. | 1.5 | 6.43 | 2.31 | 6.09 | 8.40 | 3.48 |

Table5: Drug content of chloramphenicol tablets containing 42% w/w of the various vehicles

| | *Avicel* | *Anhydrous* | *STA-R$_x$* | *Sugartab* | *Emcompress* |
|---|---|---|---|---|---|
| Mean | 96.43 | 93.12 | 102.42 | 80.21 | 91.32 |
| S.D. | 5.43 | 5.10 | 3.62 | 3.93 | 4.17 |
| C.V. | 5.64 | 5.48 | 3.54 | 4.90 | 4.57 |

Table 6: Drug content of chloramphenicol tablets containing 49% w/w of the various vehicle

| | *Avicel* | *Anhydrous lactose* | *STA-R$_x$* | *Sugartab* | *Emcompress* |
|---|---|---|---|---|---|
| Mean | 96.72 | 90.46 | 96.03 | 80.99 | 95.10 |
| S.D. | 1.83 | 2.77 | 3.58 | 6.31 | 2.38 |
| C.V. | 1.89 | 3.06 | 3.73 | 7.79 | 2.50 |

Table 7: Mean drug content of chloramphenicol tablets containing various concentrations of the different vehicles.

| *% of vehicle used* | *Avicel* | *Anhydrous lactose* | *STA-R$_x$* | *Sugartab* | *Emcompress* | *Celutab* |
|---|---|---|---|---|---|---|
| 19% | 107.10 | 103.25 | Non-compressible | Non-compressible | 105.71 | 99.08 |
| 32% | 96.39 | 9[illegible]45 | 111.82 | 88.08 | 92.71 | 93.55 |
| 42% | 96.43 | 93.12 | 102.42 | 80.21 | 91.32 | ----- |
| 49% | 96.72 | 96.46 | 96.03 | 80.99 | 95.10 | ----- |
| Mean | 99.16 | 96.32 | 103.42 | 83.09 | 96.21 | 96.32 |
| S.D. | 5.30 | 4.94 | 7.94 | 4.34 | 6.52 | 3.91 |

## REFERENCES

1) *K.A. Khan and C.T. Rhodes, Can. J. Pharm. Sci., 8, 1, (1973).*

2) *N.L. Henderson, and A.J. Brano, J. Pharm. Sci., 54, 1336 (1970).*

3) *M.A. Kassem, Master Thesis Cairo University (1975).*

4) *A.M. Sakr, A.A. Kassem, S.A.A. and A.H. Shalaby , Can., J. Pharm. Sci., 8, 6, (1973).*

5) *A.M. Sakr, A.A.Kassem, A.E. Aboutaleb, S.H. Khidr, and S.E. Saleh, Egypt J. Pharm. Sci., 17, 335, (1976).*

6) *N. Kitamori and T. Makino, J. Pharm. Pharmac., 31, 505, (1979).*

7) *Z.T. Chowhan and T.P. Chow, J. drug development & Industrial Pharmacy, 6, 1,(1980) .*

# تاثير الصواغات المختلفة على توازن المحتوى الدوائى لاقراص الكورامفينكول المحضرة بطريقة الكبس المباشر

احمد السيد ابو طالب - صالح اسماعيل صالح
قسم الصيدلة الصناعية - كلية الصيدلة - جامعة اسيوط

حضرت اقراص الكورامفينكول باستخدام تركيزات مختلفة من صواغات الكبس المباشر ولقد وجد ان الافسيل والاستى اراكس انتج اقراص من الكورامفينكول تنطبق عليها مواصفات دستور الادوية البريطانى. ومن الناحية الاخرى وجد ان الشجرتاب وسكر اللبن الامائى والامكمبرس والسلوتاب انتج اقراصا لها وقت تفتت طويل. ولقد وجد ان ان كل الاقراص المحضرة متوازنة فى محتواها الدوائى عدا الاقراص التى تحتوى على تركيزات مختلفة من الشجرتاب وهذا يعذى الى الاختلاف فى الخواص الطبيعية بين مسحوق الكورامفينكول وبودرة الشجرتاب .

*received in 6/5/1982 & accepted in 10/6/1982*