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EFFECT OF DIRECTLY COMPRESSIBLE VEHICLES ON UNIFORMITY OF CONTENTS OF OXYTETRACYCLINE HYDROCHLORIDE TABLETS

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The effect of microcrystalline cellulose(Avicel), Anhydrous lactose U.S.P., STA-R 1500 and Celutab, on the uniformity of contents of directly compressed oxytetracycline hydrochloride tablets was studied. The vehicles were used singly or in binary mixtures in the ratios 1:1 , 3:1 and 1:3. Three different concentrations of vehicles were used plus the control 19.6, 32.6, 42% w/w . It was found that single vehicles produced uniform tablets except those containing high concentration of celutab. On the other hand the uniformity of drug contents of the tablets containing various concentrations of blends of vehicles was foud to vary according to the physical properties and the concentrations of the excipients used.

The direct compression technique is less time consuming and of lower costs than the other methods. Furthermore, few steps are used for the preparation of tablets and consequently few machinery are required. It was also reported that the pressure required to affect the desired tablet hardness is generally less with direct compression vehicles than with conventional granulations, thus resulting in both higher production rate and longer tool and

machine life[1] . Another benefits will not be subjected to moisture or heat and therefore improved the stability of the tablets produced.

Ideal direct compression vehicle should have high flowability and compressibility, should be physically, chemically, and physiologyically inert, should be stable with time and stable to air, moisture, and heat. A high capacity is also required. The vehicle should be colourless, tasteless, and ac t colourants uniformly. Furthermore, The excipient sh l possess proper mouth fell and also should be relatively inexpensive and can be reworked again[2-5].

The purpose of this work is to prepare directly compressed oxytetracycline hydrochloride tablets using various concentrations of blends of vehicles and to evaluated them with regard to their uniformity of drug contents.

EXPERIMENTAL

Materials:

Oxytetracycline hydrochloride[a], magnesium stearate[b] , fine powder, stearic acid and the following directly compressible vehicles: Avicel PH 101[c] , directly compressible starch (STA-R_x1500)[d] , Anhydrous lactose U.S.P.[e] , Celutab[f] which is defined as the spray crystallized maltose-dextrose porous spheres, Stearic acid 2% w/w was used as lubricant when STA-R_x was used as vehicle singly or in mixtures as magnesium stearate was reported to be unsuitable as lubricant for STA-R_x[6] .

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a- El Nasr Chemical and Pharmaceutical Company, Cairo, Egypt.
b- C.I.D. Co., Giza, Egypt.
c- F.M.C. Corporation, Pennsylvania, U.S.A.
e- Sheffield Chemical, N.J.
f- E. Mendell Co., Inc., Carmel, N.Y. U.S.A.

Methods

The excipients were mixed with oxytetracycline Hcl and the lubricant in a drum mixer for a period of 15 minutes. The percentage of excipient used were 42.0, 32.6 and 19.6% w/w. A Manesty F[3] single punch ecenteric compression machine was used for the manufacturing of the tablets. The machine was set to produce flat, scored, 6.4 ± 0.01 mm. Tablets. The weight of the tablets was adjusted to about 0.1 g with the best possible hardness and friability for the blend containing 100% w/w of the excipient. The manufactured tablets were evaluated for their uniformity of weight(B.P. 1973) , uniformity of thickness, hardness (Erewka), (7), friability (Roche) (8), and disinategration time(modified B.P.), according to the previously published procedures (9).

Each of Avicel, STA-R_x1500, and Anhydrous lactose and Celutab was mixed with each other in the ratio of 3:1, 1:1 and 1:3 w/w . The mixed vehicles were then incorporated with oxytetracycline Hcl in the same way as with the single excipients, and the manufactured tablets were evaluated for their physical standards as mentioned before [10].

Uniformity of drug contents:

The uniformity of drug contents of oxytetracycline hydrochloride tablets was carried using 10 tablets Individually Oxytetracycline hydrochloride content was determined spectrophotometrically by reading the absorbance at 268 nm in 0.1 N hydrochloric acid.

RESULTS AND DISCUSSION

It was found that the tablets produced using various concentrations of the directly compressible vehicles, Complied with the B.P. 1973 requirement for uniformity of drug

contents, except for those batches containing 42% w/w of celutab as shown in Table 2. It was also noticed that as the concentration of the vehicle increased in the formula, more uniform tablets were produced except in the case of celutab. This may be due to the large difference between the particle size of celutab and oxytetracycline hydrochloride , consequently segregation may occur and improper filling of the die takes place as shown in Table 1.

On using blends of vehicles for the preparation of oxytetracycline hydrochloride tablets it was found that the tablets containing various blends of vehicles with celutab produced uniform tablets except those containing low concentration (19.6% w/w) of the excipient especially in the case of blends containing Avicel/Celutabe 1:3. This was also the case with blends containing 19.6% w/w and 32.6% w/w of Avicel/STA-R_x 1:1 and Avicel/STA-R_x 1:3 respectively which may be due to variations in the physical properties between the blends and oxytetracycline Hcl. The low bulk density of Avicel and the difference in angle of repose between it and oxytetracycline Hcl powder may be responsible for the non-uniformity of these batches containing blends with Avicel as shown in Tables 1,3.

On using blends of vehicles with anhydrous lactose for the preparation of oxytetracycline Hcl tablets, it was found that all the batches produced were uniform with regard to their drug contents except those containing anhydrous lactose/ STA-R_x 1:3 in the ratio of 42% w/w. Again variations in the physical properties between the blends and the drug may be responsible for such non-uniformity as shown in Table 4.

On using various blends of vehicles with celutab for the preparation of oxytetracycline Hcl tablets it was found that the batches containing low concentration of vehicle were non-uniform especially those containing Celutab/Anhydrous lactose 1:3 and 3:1. This was also the case with Celutab/STA-R_x 1:3. The batches containing 42% w/w of Celutab/Anhydrous lactose

was also non-uniform as shown in table 5. This may be due to the large particle size of Celutab, which leads to segregation in powdered mixture.[10]

The difference in the bulk density and compactabiblity of the blends used as well as variations in the flow properties of the powdered mixtures may be responsible for such non-uniformity of certain batches especially those containing low concentrations of the excipients. It was recommended that the powders used in the direct compression technique should flow frecly and be of minimum voids to ensure coninuous and uniform fill of the die of the tablet press.[11] Other factors such as the ratio of the different vehicles in the blends and the variations physical properties between these blends and the drug may also play a part. It was reported that the powder compactability factor increased as the powder bulk density decreased and the plots of these two properties were linear at lower bulk density[12].

Table 1: Physical properlies of powdered oxytetracycline Hydrochloride and direct compression vehicles used

Material	*Average particle size (U)*	*Packed bulk density gm/ml*	*Angle of repase*	
Oxytetracycline Hydrochloride	75.00	0.72	26°	63"
Avicel pH 101	82.99	0.355	40°	00
STA-R_x1500	113.21	0.668	28°	30"
Ahydrous Lactose	185.07	0.559	40°	00"
Celutab.	342.58	0.683	31°	58"

Table 2: Uniformit y of drug contents of oxytetracycline hydrochloride tablets using single vehicles

vr vehicle composition	*Percentage of vehicle*	*Mean of drug content percent (practical)*	*Mean of drug content percent (theoretical)*	*Percent deviation from theoretical*
Anhydrous	42.0	57.00	56.98	± 0.04
	32.6	66.63	65.35	± 1.96
	19.6	85.17	78.40	± 8.64
Avicel	42.0	58.67	56.98	± 2.97
	32.6	66.61	65.35	± 1.93
	19.6	86.31	78.40	± 10.09
Celutab	42.0	71.50	56.98	± 25.48
	32.6	68.68	65.35	± 5.10
	19.6	83.36	78.40	± 6.33

Table 3: Uniformity of drug contents of oxytetracycline hydrochloride tablets containing various blends of vehicles with Avicel.

Vehicle composition	*Perentage of vehicle*	*Mean of drug content percent (Practical)*	*Mean of drug content percent (theoretical)*	*Percent deviation from theoretical*
Avicel - Celutab 1 : 1	42.0	52.20	56.98	± 8.39
	32.6	64.24	65.35	± 1.70
	19.6	73.23	78.40	+ 6.6
Avicel - Celutab 1 : 3	42.0	60.84	56.98	± 6.77
	32.6	60.41	65.35	+ 7.56
	19.6	87.44	78.40	+11.53
Avicel - Celutab 3 : 1	42.0	57.21	56.98	± 0.40
	32.6	65.41	65.35	± 0.09
	19.6	80.91	78.40	+ 3.20
Avicel - STA-R_x 1 : 1	42.0	59.23	56.98	± 3.97
	32.6	67.64	65.35	± 3.50
	19.6	69.59	78.40	+11.24
Avicel - STA-R_x 1 : 3	42.0	53.80	56.98	± 5.58
	32.6	55.56	65.35	±14.98
	19.6	73.51	78.40	+ 6.24
Avicel - STA-R_x 3 : 1	42.0	55.75	56.98	± 2.16
	32.6	61.40	65.35	± 6.04
	19.6	73.79	78.40	+ 5.88

Table 4: Uniformity of drug contents of oxytetracycline hydrochloride tablets containing various blends of vehicles with Anhydrous Lactose

Vehicle composition	*Percentage of vehicle*	*Mean of drug content percent (Practical)*	*Mean of drug content percent (theoretical)*	*Percent deviation from theoretical*
Anh. Lactose/STA-R_x 1 : 1	42.0	59.91	56.98	± 5.14
	32.6	69.53	65.35	± 6.40
	19.6	78.27	78.40	+ 0.17
Anh. Lactose/STA-R_x 1 : 3	42.0	64.30	56.98	±12.85
	32.6	64.15	65.35	± 1.84
	19.6	81.28	78.40	+ 3.67
Anh. Lactose/STA-R_x 3 : 1	42.0	58.00	56.98	± 1.79
	32.6	69.81	65.35	± 6.82
	19.6	81.42	78.40	+ 3.85

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تأثير مخاليط السواغات على تجانس محتويات اقراص هيدروكلوريد اوكسى تتراسيكلين المحضرة بالكبس المباشر

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تم دراسة تاثير بعض مواد الكبس المباشر للاقراص وهى افيسيل ، سكر اللبن اللاماتى ، استاراكس ١٥٠٠ وسليوتاب على تجانس محتويات اقراص ايدروكلوريد اوكسى تتراسيكلين .

وقد استخدمت هذه السواغات بمفردها او مع بعضها بنسب مختلفة وهى ١:١ ، ١:٣ ، ٣:١ وذلك بنسب مختلفة بالنسبة للمادة الدوائية .

وقد وجد ان السواغ المنفرد يعطى اقراصا متجانسة ماعدا التى تحتوى على نسبة عالية من السليوتاب . كما تبين اختلاف تجانس محتويات الاقراص عند استخدام مخاليط من السواغات، واختلف ذلك حسب الصفات الفيزيائية ونسبة السواغ المستخدم .

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