Available online at www.sciencedirect.com
ScienceDirect
European Journal of Pharmaceutics and Biopharmaceutics 67 (2007) 253–259
European Journal of Pharmaceutics and Biopharmaceutics
www.elsevier.com/locate/ejpb

Research paper

Formulation and evaluation of dried yeast tablets using different techniques

Abdullah M. Al-Mohizea *, Mahrous O. Ahmed, Fahad I. Al-jenoobi, Gamal M. Mahrous, Aly A. Abdel-Rahman

Department of Pharmaceutics, King Saud University, Riyadh, Saudi Arabia

Received 4 October 2006; accepted in revised form 14 December 2006
Available online 23 December 2006

Abstract

The aim of this study was to prepare and evaluate dried yeast tablets using both direct compression and dry granulation techniques in comparison with the conventional wet granulation as well as commercial product. Wet granulation technique is not favorable for producing the yeast tablets due to the problems of color darkening and the reduction of the fermentation power of the yeast as a result of the early start of the fermentation process due to the presence of moisture. Twenty six formulae of dried yeast tablets were prepared and evaluated. Certain directly compressible vehicles were employed for preparing these tablets. The quality control tests (weight uniformity, friability, disintegration time and hardness) of the prepared dried yeast tablets were performed according to B.P. 1998 limits. All batches of the prepared tablets complied with the B.P. limits of weight uniformity. Moreover, small values of friability % (1% or less) were obtained for all batches of dried yeast tablets with acceptable hardness values, indicating good mechanical properties which can withstand handling. On the other hand, not all batches complied with the limit of disintegration test which may be attributed to various formulation component variables. Therefore, four disintegrating agents were investigated for their disintegrating effect. It was found that the method of preparation, whether it is direct compression, dry granulation or wet granulation, has an effect on disintegration time of these dried yeast tablets and short disintegration times were obtained for some of the formulae. The shortest disintegration time was obtained with those tablets prepared by direct compression among the other techniques. Therefore, the direct compression is considered the best technique for preparation of dried yeast tablets and the best formula (which showed shorter disintegration time and better organoleptic properties than the available commercial yeast tablets) was chosen. Drug content for dried yeast granular powder, and the chosen best prepared formula, was determined by gas chromatography (GC). It was found that this formula gave the same alcohol content produced by an equal amount of the dried yeast granular powder. This result in conjunction with weight uniformity indicated drug content uniformity of the prepared dried yeast tablets.

Keywords: Yeast; Direct compression; Wet granulation; Dry granulation; Formulation; Tablets

1. Introduction

The disintegration of compressed tablets into granules or individual particles is a rate-limiting step for the dissolution of drugs. A large number of publications have been dedicated to study many disintegrants of different types such as sodium starch glycolate (Explotab) [1], cyclodextrin polymer [2], crosslinked carboxymethyl cellulose (Ac-Di-Sol) [3,4], crosslinked polyvinylpyrrolidone (Polyplasdone XL) [5] and formaldehyde crosslinked gelatin (Esma-Spreng) [6]. Formulations of tablets involve the choice of suitable diluents, disintegrants, lubricants, coloring agents, flavoring agents, etc., and determination of their optimum proportions. The organoleptic properties are important in case of the formulation of chewable tablets and in case of

* Corresponding author. Department of Pharmaceutics, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia. Fax: +966 1 4676295.
E-mail address: amohizea@ksu.edu.sa (A.M. Al-Mohizea).

0939-6411/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.ejpb.2006.12.011

tablets which has nauseous bad odor [7]. There are different techniques of tablet preparation including wet granulation, dry granulation, and direct compression. Each of these techniques has its own characteristics, but direct compression technique has low labor input and requires fewest processing steps, beside the enhanced stability of moisture and heat-sensitive drugs [8]. In comparison to direct compression and dry granulation techniques, the wet granulation technique is unfavorable for preparation of yeast tablets because the yeast starts the fermentation process directly after the manufacturing of the tablets, and may exhaust the yeast fermentation power. In addition, the early fermentation observed after wet granulation of the yeast tablets causes darkening of the color of the produced tablets.

Dried yeast is somewhat granular powder with a characteristic odor and somewhat bitter taste. Dried yeast is used for the prevention and treatment of vitamin-B deficiency and to improve the beneficial fermentation for digestion in the GIT [9]. As a dietary supplement it has been given in the following doses: 1–2.5 g daily in milk for infants, 4–6 g for children and 6–8 g for adults. In conditions of severe vitamin-B deficiency, such as beri-beri, pellagra or ariboflavinosis, adults may be given doses up to 30 g daily. It may be administered as tablets or as powder. Cholesterol assimilation by yeast strains grown in laboratory media under conditions typically found in the GIT of humans has been reported [10]. In this respect, the ingestion of yeast which showed some probiotic properties can be considered as a natural way to reduce cholesterol uptake.

The aim of this study was to formulate and evaluate yeast tablets using direct compression and dry granulation techniques in comparison with conventional wet granulation technique. Direct compression and dry granulation techniques were selected for the production of yeast tablets to avoid the previously mentioned drawbacks of the wet granulation technique. Also, the effect of various disintegrants on the disintegration time of prepared yeast tablets was studied. Finally, the fermentation power of the best produced formula will be evaluated in comparison with the granular powder of yeast by GC method.

2. Materials and methods

2.1. Materials

Dried yeast granules were purchased from the local market (Marcq, France). Dry yeast commercial tablets were obtained from Echart Corp. USA. Avecil PH 101 (microcrystalline cellulose), spray dried lactose and aerosil were purchased from Winlab (Maidenhead, UK). Starch was purchased from BDH Laboratory Supplies (Poole, England). Magnesium stearate was purchased from Riedel-DeHuen AG, Seeleze, Hannover. Microcelac 100 (a spray dried mixture of 75 parts lactose monohydrate and 25 parts microcrystalline cellulose), Cellactose 80 (a spray dried mixture of 75% lactose and 25% cellulose), Starlac (a spray dried mixture of 85% lactose and 15% starch), Tablettose 80 (brand name for agglomerated lactose), Presmalac 40 (brand name for a sieved lactose), Granulac 70 (brand name for a fine milled lactose) and Capsulac 60 (brand name for a sieved lactose) were supplied from Molkerei Meggle Wasserburg GmbH & Co. KG (Germany). All solvents used for chromatographic determinations were of HPLC grade. All other reagents and solvents were of analytical grade.

2.2. Methods

2.2.1. Preparation of yeast tablets by the direct compression technique

Components of each formula as shown in Table 1 were mixed in turbula mixer (type S27, Erweka, Apparatebau, Germany) and then directly compressed into tablets using a single punch tablet machine (type EKO, Erweka, Apparatebau, Germany) using 11 mm concaved punches. Tablets' crushing strength was kept within the range of 4–8 kp and tablet weights were kept within 3% of the average weight of each formula.

2.2.2. Preparation of yeast tablets by the dry granulation technique

Components of each formula as shown in Table 2 were mixed in turbula mixer (type S27, Erweka, Apparatebau, Germany) and then compressed using a single punch tablet machine (type EKO, Erweka, Apparatebau, Germany) using 16 mm flat punches. The produced slugs were then crushed into dry granules and passed through sieve size 800 μm and retained on sieve size 250 μm. The rest of disintegrant and lubricant were added, mixed in turbula mixer, and then compressed by a single punch tablet machine (type EKO, Erweka, Apparatebau, Germany) using 11 mm concave punches. Tablet crushing strength was kept within the range of 4–8 kp and tablet weights were kept within 3% of the average weight of each formula.

2.2.3. Preparation of yeast tablets by the wet granulation technique

Dried yeast granules were milled, and mixed with the diluent and half the amount of the disintegrant (Table 2). Granulation was carried out using PRS planetary mixer (Erweka, Apparatebau, Germany) at a speed of 30 rpm. Binder solution (Alcohol 96% containing 5% PVP K90) was gradually added to the powder mixture until the formation of coherent mass. The obtained mass was then passed through a 10-mesh sieve (2 mm) and then dried at 40 °C overnight. The obtained granules were passed through 20-mesh sieve (800 μm) then, the other half of the disintegrant and the required amount of the lubricant were added and then the blend was compressed as in direct compression method mentioned above.

2.2.4. Particle size analysis

The average particle size of the dried yeast granular powder was determined by sieve analysis using 100 g of

Table 1
Dried yeast tablet formulations prepared by direct compression technique

Ingredients	Weight of ingredients (mgs) per tablet Formula No.													
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14
Dry yeast	350	350	350	350	350	350	350	350	350	350	350	350	350	350
Mag. Stearate	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Aerosil	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Avecil PH 101	200	–	100	–	–	–	–	–	–	–	200	200	200	200
Spray dried lactose	–	200	100	–	–	–	–	–	–	–	–	–	–	–
Presmalac 40	–	–	–	200	–	–	–	–	–	–	–	–	–	–
Tablettose 80	–	–	–	–	200	–	–	–	–	–	–	–	–	–
Microcelac 100	–	–	–	–	–	200	–	–	–	–	–	–	–	–
Capsulac 60	–	–	–	–	–	–	200	–	–	–	–	–	–	–
Starlac	–	–	–	–	–	–	–	200	–	–	–	–	–	–
Cellactose	–	–	–	–	–	–	–	–	200	–	–	–	–	–
Granulac 70	–	–	–	–	–	–	–	–	–	200	–	–	–	–
Corn starch	–	–	–	45	45	45	45	45	45	45	45	–	–	–
Cross povidone	–	–	–	–	–	–	–	–	–	–	–	45	–	–
Cross carmellose	–	–	–	–	–	–	–	–	–	–	–	–	45	–
Explotab	–	–	–	–	–	–	–	–	–	–	–	–	–	45
Total tablet weight (mg)	555	555	555	600	600	600	600	600	600	600	600	600	600	600

Table 2
Dried yeast tablet formulations prepared by dry and wet granulation techniques

Ingredients	Weight of ingredients (mgs) per tablet Formula No.											
	#15	#16	#17	#18	#19	#20	#21	#22	#23[a]	#24	#25[a]	#26
Dry yeast	350	350	350	350	350	350	350	350	350	350	350	350
Mag. Stearate	4	4	4	4	4	4	4	4	4	4	4	4
Aerosil	1	1	1	1	1	1	1	1	1	1	1	1
Avecil PH 101	200	200	200	200	–	–	–	–	100	200	200	100
Spray dried lactose	–	–	–	–	–	–	–	–	100	–	–	100
Presmalac 40	–	–	–	–	200	–	–	–	–	–	–	–
Microcelac 100	–	–	–	–	–	200	–	–	–	–	–	–
Starlac	–	–	–	–	–	–	200	–	–	–	–	–
Cellactose 80	–	–	–	–	–	–	–	200	–	–	–	–
Corn starch	45	–	–	–	–	–	–	–	60	–	–	60
Cross povidone	–	45	–	–	–	–	–	–	–	–	–	–
Cross carmellose	–	–	45	–	–	–	–	–	–	–	–	–
Explotab	–	–	–	45	45	45	45	45	–	–	45	–
PVP K90	–	–	–	–	–	–	–	–	16	–	16	–
Total tablet weight (mg)	600	600	600	600	600	600	600	600	631	555	616	615

[a] Wet granulation formula.

the test material and sieves of US standard [11]. Sieves are arranged in screen opening from 1000 to 180 μm. The test material was placed on the top sieve and the sieve set was mechanically shaken for 10 min on shaker (Rota C30, Germany). The fraction retained on each screen was weighted and the average particle size was calculated.

2.2.5. Bulk density (Carr's index, I)

The bulk density of the dried yeast granular powder was determined by filling the material into a tarred graduated cylinder to the 100 ml mark. The bulk density (D_b) was calculated as the ratio of the sample weight to the sample volume. The cylinder was then tapped until constant volume was achieved and the tap density (D_t) was calculated. Carr's index (I) was calculated using the following formula:

$$I = [1 - D_b/D_t] \times 100.$$

2.2.6. Angle of repose (θ)

Angle of repose of the dried yeast granular powder was measured using a glass funnel and a graph paper. The distance between funnel and graph paper was set to 2 cm (h), the dried yeast material was allowed to flow through the funnel onto the graph paper. The reading of the radius (r) at the base of the cone formed by the powder on the

graph paper was recorded. Then, the angle of repose was calculated using the following formula:

$\theta = h/r.$

2.2.7. Evaluation of the produced yeast tablets

The obtained tablets of dried yeast were evaluated with regard to weight uniformity and disintegration time according to the B.P. 1998. The crushing strength was determined using hardness tester (type TBH 28, Erweka, Apparatebau, Germany) and the friability was determined using Roche friability tester (Erweka, Apparatebau, Germany).

2.2.8. Determination of alcohol content produced from yeast fermentation

One gram of the dried yeast granular powder or its equivalent amount from prepared tablets of formulae 14 and 23 was suspended in 20 ml of sterile distilled water in Sterilin tubes (Sterilin Ltd, England). These tubes were incubated at 35 °C for 48 h. The alcohol content produced from yeast fermentation was measured in supernatant fluid by gas chromatography [12]. This method depends on the determination of the ethyl alcohol amount produced from the fermentation of yeast in vitro [10,12].

2.2.9. Gas chromatography (GC)

Analysis was carried out on a capillary column HP 5890 gas chromatography system. The solid phase was crossbonded phenylmethyl polysiloxane. The carrier gas was helium 70 °C isothermally. The injection temperature was 150 °C and the flame ionization detector temperature was 250 °C. The injection sample volume was 1 μl and the sampling rate was 1.5625 pts/s.

2.2.10. Statistical analysis

Statistical significance was evaluated using ANOVA only for formulae that show lower disintegration time than the commercial tablets using prism software ver. 3.0 (GraphPad Software Inc., USA). The differences were considered significantly different when the p-value $\leqslant 0.05$.

3. Results and discussion

Preformulation study showed that average particle size of dried yeast powder was 398 μm as determined by sieving analysis method. Moreover, the angle of repose and Carr's index were determined and found to be 28° and 5.5%, respectively. Although the dried yeast powder possessed good flow properties as obvious from the previous data, it cannot be easily compressed alone by direct compression technique since the produced tablets showed elastic deformation and cannot withstand handling. Therefore, directly compressible vehicles were used to overcome such difficulties. Optimum amount (200 mg) of directly compressible diluents was added to each formula of dried yeast tablets. This amount was chosen based on our observation that smaller amount of the diluent always produced weak tablets. Also, a larger amount of the diluent will produce large-sized tablets that are difficult to be swallowed. The amounts of the disintegrant and the lubricant (45 and 5 mg, respectively) were added to each formula and these amounts represent 7.5% and 0.8% of tablet weight, respectively, which are within the commonly used range of both the disintegrant (5–10%) and the lubricant (0.5–2%).

Various formulae of dried yeast tablets were prepared by direct compression (Table 1), dry granulation and wet granulation techniques (Table 2). The produced tablets were compared with each other as well as with the commercial product. Different directly compressible vehicles were tested (Avecil PH 101, spray dried lactose, Tablettose 80, Cellactose 80, Starlac, Microcelac 100, Presmalac 40, Capsulac 60 and Granulac 70). Tables 1 and 2 show the composition of each formula of dried yeast tablets. Tables 3 and 4 show the quality control tests of dried yeast tablets. All batches of the prepared tablets complied with the B.P. limits [13] of weight uniformity. Moreover, acceptable values of friability (loss % $\leqslant$1) were obtained for all batches of dried yeast tablets with suitable hardness values, indicating good mechanical properties which can withstand handling. On the other hand, not all batches of the prepared yeast tablets complied with the limit of disintegration test of the B.P. 1998 (15 min), which may be attributed to various characteristics of diluents used. Hence, the influence of some disintegrants (explotab, cross carmellose, cross povidone and corn starch) on the disintegration time of the prepared dried yeast tablets was investigated. Table 3 shows the effect of corn starch on the disintegration time of dried yeast tablets of formula No. 4 to formula No. 11 prepared by direct compression technique. Reduction of the disintegration time was observed with formulae No. 5, 8, 9, and 11 (27, 25, 30 and 18 min, respectively) compared to formulation containing no disintegrants (formulae No. 1, 2 and 3 with an average disintegration time of 40 min). This may be due to the different characteristics of diluents used. Pronounced effect of corn starch was observed in reducing the disintegration time from 40 min (formula No. 1) to 18 min (formula No. 11) prepared by direct compression (Table 3) and from 52 min (formula No. 24) to 30 min (formula No. 15) prepared by dry granulation (Table 4), but still outside the limits of 15 min of the B.P. Therefore, other disintegrants (cross povidone, cross carmellose and explotab) were tried, and their effect on the disintegration time of formula No. 1 (prepared by direct compression) or formula No. 24 (prepared by dry granulation) is shown in Tables 3 and 4. Disintegration time within the 15 min limit of the B.P. 1998 was observed with formulae No. 12, 13 and 14 (direct compression) and formulae No. 16, 17 and 18 (dry granulation) in presence of cross povidone, cross carmellose or explotab, respectively. These results indicate that direct compression and dry granulation techniques are superior to wet granulation technique in obtaining dried yeast tablets with shorter disintegration time. Comparatively, direct compression technique produced yeast tablets,

Table 3
Physical characteristics of the dried yeast tablets prepared by direct compression technique

Test	Formula No.													
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14
Hardness (kp) ± SD	7.84 ± 0.8	4.1 ± 0.5	6.8 ± 0.7	5.64 ± 0.6	6.0 ± 0.8	5.3 ± 0.6	5.4 ± 0.8	5.8 ± 0.6	6.1 ± 0.7	6.2 ± 0.8	5.02 ± 0.6	6.12 ± 0.8	4.93 ± 0.8	5.2 ± 0.6
Friability %	1	0.26	0.4	0.18	0.30	0.20	0.33	0.20	0.43	0.21	0.31	0.21	1.0	0.39
Weight uniformity average weight (mg) ± SD	556 ± 6	560 ± 6	554 ± 9	612 ± 9	609 ± 7	609 ± 12	598 ± 10	605 ± 11	606 ± 13	610 ± 12	599 ± 10	603 ± 11	611 ± 12	607 ± 11
Actual weight range (mg)	548–562	551–566	544–563	590–621	585–616	580–623	579–619	589–619	588–620	592–625	576–620	589–618	590–630	589–622
Acceptable weight range (mg)	528–584	532–588	526–581	581–642	578–639	578–639	570–628	575–635	576–636	580–640	569–629	573–633	580–641	576–637
Disintegration time (min) ± SD	40 ± 4	45 ± 4	35 ± 3	44 ± 3	27 ± 2	38 ± 3	44 ± 4	25 ± 2	30 ± 3	40 ± 3	18 ± 2	3[a] ± 1	10 ± 1	5[a] ± 1

[a] Significantly different from the commercial tablets (ANOVA was done for formulae that have lower disintegration time than commercial tablets).

Table 4
Physical characteristics of the dried yeast tablets prepared by dry or wet granulation techniques

Test	Formula No.												
	#15	#16	#17	#18	#19	#20	#21	#22	#23[b]	#24	#25[b]	#26	Commercial Tablets
Hardness (kp) ± SD	5.82 ± 0.6	6.32 ± 0.8	5.54 ± 0.7	5.6 ± 0.6	5.6 ± 0.6	6.5 ± 0.8	5.4 ± 0.6	5.8 ± 0.5	5.4 ± 0.5	8.5 ± 0.7	5.8 ± 0.6	6.2 ± 0.8	4.8 ± 0.5
Friability %	0.3	0.16	0.9	0.37	0.28	0.6	0.8	0.3	0.63	0.8	0.4	0.6	0.37
Weight uniformity average weight (mg) ± SD	606 ± 11	608 ± 12	607 ± 10	609 ± 12	603 ± 10	601 ± 13	605 ± 10	602 ± 12	628 ± 10	560 ± 8	628 ± 11	621 ± 13	426 ± 7
Actual weight range (mg)	588–620	591–621	588–623	585–628	581–619	578–618	590–615	589–618	618–639	549–568	610–640	605–635	419–434
Acceptable weight range (mg)	576–637	577–638	576–637	578–639	573–633	571–631	575–635	572–638	597–659	528–548	597–659	590–652	405–447
Disintegration time (min) ± SD	30 ± 3	8[a] ± 1	15 ± 2	7[a] ± 1	8[a] ± 1	7[a] ± 1	9[a] ± 1	8[a] ± 1	40 ± 3	52 ± 4	18 ± 2	31 ± 3	12 ± 2

[a] Significantly different from the commercial tablets (ANOVA was done only for formulae that have lower disintegration time than commercial tablets).
[b] Wet granulation formula.

Table 5
Effect of the preparation method on the disintegration time of the prepared dried yeast tablets

Formula No.	Disintegration time (min)
Formula 1 prepared by Direct compression	40
Formula 24 prepared by Dry granulation (same content as formula 1)	52
Formula 11 prepared by Direct compression	18
Formula 15 prepared by Dry granulation (same content as formula 11)	30
Formula 12 prepared by Direct compression	3
Formula 16 prepared by Dry granulation (same content as formula 12)	8
Formula 13 prepared by Direct compression	10
Formula 17 prepared by Dry granulation (same content as formula 13)	15
Formula 14 prepared by Direct compression	5
Formula 18 prepared by Dry granulation (same content as formulae 14 and 25)	7
Formula 25 prepared by Wet granulation (same content as formulae 14 and 18)	18
Formula 23 prepared by Wet granulation	40
Formula 26 prepared by Dry granulation	31
Commercial tablet	12

formulae No. 11, 12, 13 and 14, with disintegration time shorter than that of formulae No. 15, 16, 17 and 18 prepared by dry granulation. The efficiency of the used disintegration agents toward the disintegration of the produced dried yeast tablets can be arranged in the following order: explotab > cross povidone > cross carmellose > corn Starch. Therefore, explotab was selected to be included with other formulae (No. 19, 20, 21 and 22) containing different diluents other than Avecil PH 101 (Presmalac 40, Microcelac 100, Starlac and Cellactose 80, respectively) to study its effect on disintegration time. It was found that explotab, as a disintegrant, was effective in obtaining shorter disintegration times (8, 7, 9 and 8 min) which are within the 15 min limits for the previously mentioned formulae No. 19, 20, 21 and 22, respectively, although they were prepared by dry granulation method. Hence, explotab can be used successfully as a super-disintegrating agent for tablets prepared by dry granulation technique. Explotab is known to be widely used as a superdisintegrant in tablets prepared by both direct compression and wet granulation techniques [1].

Table 5 shows the effect of different preparation methods on the disintegration time of dried yeast tablets. It was found that the method of preparation has an effect on the disintegration time as confirmed from the shortest disintegration time of the dried yeast tablets prepared by direct compression among the other methods. For example, the disintegration time for formula No. 14 of prepared yeast tablets (direct compression), formula No. 18 (Dry granulation) and formula No. 25 (wet granulation) was 5, 7 and 18 min, respectively. The shortest disintegration time of yeast tablets produced by direct compression can be attributed to absence of granular effect and the rapid hydration of these tablets when they come in contact with water. Therefore, the direct compression technique is the best method for preparing the dried yeast tablets and this was represented by formula No. 14.

In comparison to the commercial product, our prepared dried yeast tablets were better in their physical properties (Table 4). Our prepared dried yeast tablets have a shorter disintegration time. Also, they have higher hardness values than the commercial ones. In terms of friability, our prepared yeast tablets, even those prepared by direct compression, have lower friability than the commercial ones. Moreover, the organoleptic properties of the prepared dried yeast tablets are better than those of the commercial tablets, for example, the prepared tablets have good odor and taste, and white color, whereas the commercial tablets have nauseous odor, bitter taste and dark brown color. This observation could be a result of some factors including the addition of diluents that have acceptable taste and also the absence of yeast fermentation of our produced tablets. Therefore, our dried yeast formulations are promising to be prepared as chewable tablets as they have palatable taste as proven by the opinion of three volunteers after being chewed in mouth and ingested.

Yeast fermentation activity (as an indicator of the yeast content) of selected prepared yeast tablets (formulae No. 14 and 23) and the dried yeast granular powder was determined by the production of ethyl alcohol via fermentation. The alcoholic content resulting from the fermentation process was determined by gas chromatography [10,12]. It was found that the formula No. 14 gave the same alcohol content (18.73%) produced by an equivalent amount of the dried yeast granular powder. This result in conjunction with weight uniformity indicates the uniformity of drug content of our developed dried yeast tablets and the good fermentation power of the produced tablets.

Acknowledgement

The authors are grateful to the Research Center, College of Pharmacy, King Saud University, for the financial support for this project (C.P.R.C 190).

References

[1] N.A. Aldouri, M.O. Ahmed, S.K. El-Jamal, Study of effect of various disintegrants on the physical properties and dissolution behavior of the directly compressed theophylline tablets, Bull. Pharm. Sci. Assuit Univ. 25 (1) (2003) 23.
[2] E. Fenyvest, B. Antal, B. Zsadon, J. Szejtli, Cyclodextrin polymer: a new tablet disintegrating agent, Pharmazie 39 (1984) 473.
[3] D. Gissinger, A. Stamm, Effect of compression force, humidity and disintegrant concentration on the disintegration and dissolution of direcly compressed furosemide tablets using croscarmellose sodium as disintegrant, Pharmaz. Ind. 42 (1980) 189.
[4] E.A. Gorman, C.T. Rhodes, E.M. Rudnic, An evaluation of croscarmellose as a tablet disintegrant in direct compression systems, Drug Dev. Ind. Pharm. 8 (1982) 397.
[5] W.A. Ritschel, P.W. Luecker, W. Rendt, Pharm. Ind. 44 (1982) 184.
[6] E. Graf, A.H. Ghanem, A. Saker, H. Mahmoud, Pharm. Ind. 43 (1981) 576.
[7] M.F. Al-Omran, S.A. Alsuwayeh, A.M. El-Helw, S.I. Saleh, Formulation and physicochemical evaluation of diclofenac sodium chewable tablets, S. Pharm. J. 10 (4) (2002) 177.
[8] Remington: The Science and Practice of Pharmacy, 19th ed., Mack Publishing Company, 1995.
[9] Martindale: The Extra Pharmacopoeia, 28th ed., The Pharmaceutical Press, London, 1982, p. 1641.
[10] E.A. Psomas, D.J. Fletouris, E. Litopoulou-Tzonetaki, N. Tzanetakis, Assimilation of cholesterol by yeast strains isolated from infant feces and Feta cheese, J. Dairy Sci. 86 (2003) 3416.
[11] United States Pharmacopoeia (USP), Convention Inc., MD, USA, 2000.
[12] F.W. Bai, L.J. Chen, Z. Zhang, W.A. Anderson, M. Moo-Young, Continuos ethanol production and evaluation of yeast cell lysis and viability loss under very high gravity medium conditions, J. Biotechnol. 110 (2004) 287.
[13] British Pharmacopoeia (B.P.), Pharmaceutical Press, London, UK, 1998.