[Chem. Pharm. Bull. 30(11)4216—4218(1982)]

Directly Compressed Tablets containing Chitin or Chitosan in Addition to Mannitol[1)]

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(Received May 28, 1982)

As a part of a series of studies on pharmaceutical applications of chitin and chitosan, the fluidity and compressibility of combined powders of mannitol with chitin and chitosan, as well as the disintegration properties of tablets made from these powders were investigated in comparison with those of crystalline cellulose with mannitol.

The fluidity of the combined powders with chitin and chitosan was a little greater than that of the powder with crystalline cellulose. At more than 30% addition of chitin, chitosan or crystalline cellulose, tablets were easily formed. Tablets containing less than 60% chitin or chitosan passed the disintegration test of JP X. It is suggested that chitin and chitosan, as well as crystalline cellulose, may be suitable as diluents for chewable, sublingual or oral mucosal tablets prepared by direct compression processes.

Keywords——chitin; chitosan; crystalline cellulose; mannitol; direct-compression; tablet

Chitin [(1→4)-2-acetamido-2-deoxy-β-D-glucan] is a widely occurring, natural structural material, and chitosan [(1→4)-2-amino-2-deoxy-β-D-glucan] can be obtained by alkaline deacetylation of chitin.[3)]

Chitin and chitosan are biodegradable by lysozyme, and do not present any biological hazard. They have been reported to be useful for pharmaceutical preparations.[3,4)]

In this study, with a view to the application of chitin and chitosan to chewable, sublingual or oral mucosal tablets, following our work on directly compressed tablets containing chitin or chitosan in addition to lactose or potato starch,[4b)] the fluidity and compressibility of combined powders of mannitol with chitin (mannitol/chitin) and with chitosan (mannitol/chitosan), as well as the disintegration properties of tablets made from these powders, were investigated in comparison with those of combined powders of mannitol with crystalline cellulose (MCC).[5)]

Experimental

Materials——The same chitin, chitosan and MCC as described in the previous paper[4b)] were used. Mannitol of JP X grade, supplied by Iwaki Seiyaku Co., Ltd. was used after passage through a 200-mesh sieve. Mixing of powders was carried out in a Tsutsui V-shaped blender for 30 min at 50 rpm.

Measurement of Fluidity——The angle of repose and the minimum orifice diameter for flow were measured in the same way as described in the previous paper.[4b)]

Tablet-making by Direct Compression——Flat-faced tablets of 300 mg weight, 13 mm diameter and about 1.7 mm thickness were made in the same way as described in the previous paper.[4b)]

Measurement of Hardness of Tablets——A Kiya hardness tester, which can be applied to measure hardness below 20 kg at a relative humidity between 55 and 65%, was used.

Measurement of Disintegration of Tablets——A Toyama Sangyo T-2HS type disintegration tester was used according to the method described in JP X using water as the test fluid.

Results and Discussion

The angle of repose and the minimum orifice diameter for flow of mannitol/chitin, mannitol/chitosan and mannitol/MCC are shown in Figs. 1 and 2. It was found that the decrease of the angle of repose of powders with the addition of chitin or chitosan was a little larger than that with the addition of MCC. As regards the decrease of the minimum orifice diameter for flow

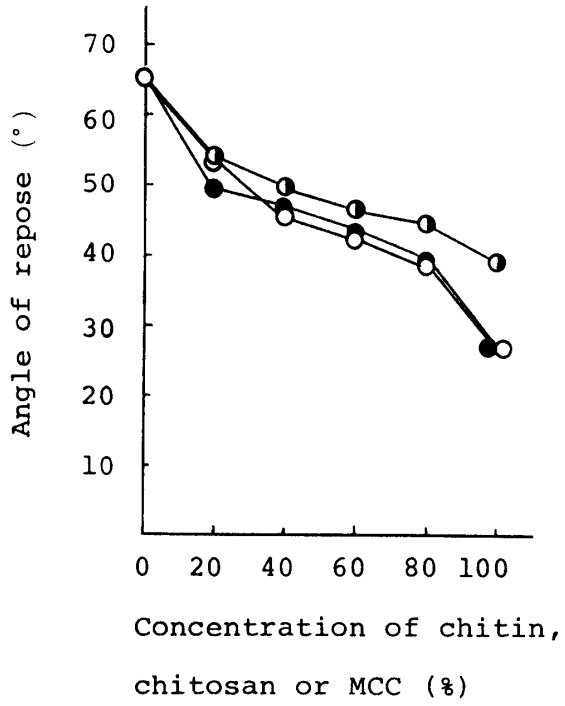

Fig. 1. Relation between Angle of Repose and Concentration of Chitin, Chitosan or MCC added to Mannitol Powder

○ : chitin; ● : chitosan, ◑ : MCC. Each point represents the mean of 3 determinations.

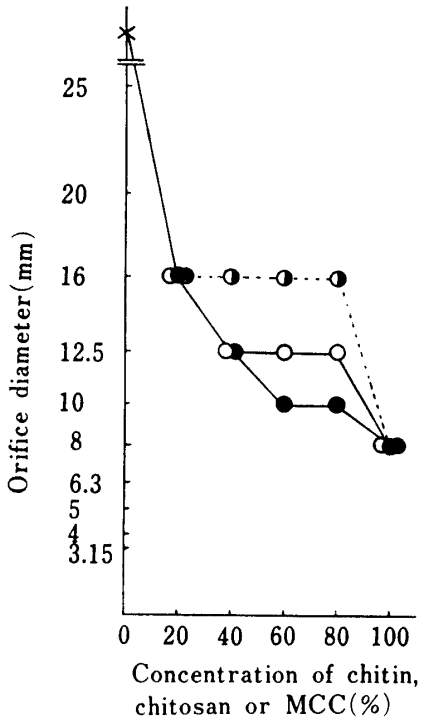

Fig. 2. Relation between Minimum Orifice Diameter and Concentration of Chitin, Chitosan or MCC added to Mannitol Powder

—○— : chitin; —●— : chitosan; ···◑··· : MCC; × : above 25 mm. Each point represents the mean of 3 determinations.

with the addition of chitin, chitosan and MCC, the same tendency was observed as in the case of the angle of repose, as shown in Fig. 2. These results indicate that the fluidity of the combined powders with chitin and chitosan was a little greater than that of the powder with crystalline cellulose, and that the very poor fluidity of mannitol was somewhat improved y the addition of chitin or chitosan.

The hardness of tablets of mannitol/chitin, mannitol/chitosan and mannitol/MCC increased with the addition of chitin, chitosan or MCC, as shown in Fig. 3. Addition of less than 20% additive resulted in failure of tablet formation because of crumbiling and chipping. Mannitol has been reported to be difficult to compress into tablets, but the addition of MCC made tablet formation possible.[5] The results shown in Fig.3 indicate that the addition of chitin and chitosan to mannitol also made tablet formation possible. Concerning the lubricating properties, the same tendency was observed qualitatively as in the previous paper,[4b] although the ejection force of the tablet was not measured in this study.

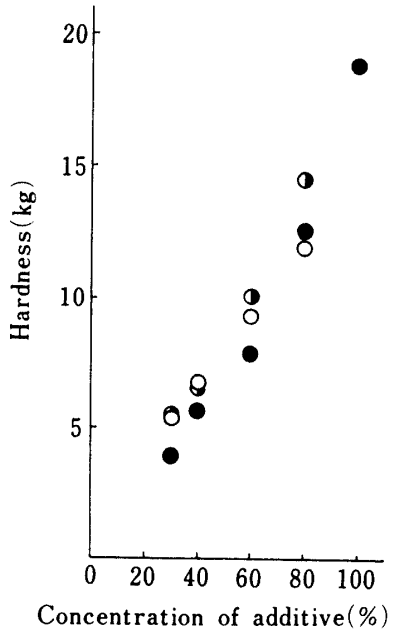

Fig. 3. Reaction between Tablet Hardness and Concentration of Additive

○ : chitin; ● : chitosan; ◑ : MCC. Each point represents the mean of 5 determinations.

As regards the relation between disintegration time of tablets and the concentration of additive, tablets containing less than 80% chitin, chitosan or MCC (exept for 80% addition of chitosan) were disintegrated within 1 min. A tablet containing 80% chitosan remained on the mesh of the tester after 60 min, and this is considered to be the critical disintegration time concentration.[4b]

Since chitin and chitosan are biodegradable by lysozyme and are inexpensive, these polymers, as well as MCC, may be suitable for use as diluents for chewable, sublingual or oral mucosal tablets prepared by direct compression processes.

Acknowledgement The authors are very grateful to Miss Kayoko Kambai and Mr. Takashi Teshigawara for their assistance in the experimental work.

References and Notes

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