STUDIES ON MODIFIED GLADIOLUS STARCH

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ABSTRACT

Gladiolus starch was modified by the action of heat to produced two batches of pyrodextrins. The produced pyrodextrins were subjected to some pharmacopoeial tests for identification, and some physicotechnical tests designed to establish their possible relevance in certain pharmaceutical formulations. Such parameters as microscopy, density, solubility, moisture content, reducing sugar content, surface tension of 2.5% w/v solution and rheological properties were evaluated. The result of the physicotechnical properties indicated that these two pyrodextrins could be a versatile pharmaceutical tabletting aid ,possessing multifunctionality.

Keywords: Gladiolus starch; Pyrodextrin; Physicotechnical properties; Excipient

INTRODUCTION

Modification is done by chemical treatments or other methods in order to obtain combination of properties suitable for specific applications. For many industrial applications, the properties of natural starches are changed by various treatments such as heat, acid, enzymes or oxidizing agents. A wide variety of new properties may thus be induced. These modified starches are often called dextrins [1] or pyrodextrins if the conversion was brought about by the action of heat. Heat induces hydrolysis, rearrangement, and repolymerization of the native starch [2, 3]. The result of this is products that do not retrograde easily and with excellent stability. Solutions of dextrins are more sticky and tacky and dry faster than the native starches [3]. Dextrins are used as binders, thickening agents for suspensions and emulsions, sugar coating ingredients and as direct compression filler/binder [4-9]. This research work was aimed at production and evaluation of dextrins from the corms of Gladiolus actinomorphanthus plan (Fam. Iridaceae) for possible pharmaceutical applications. Gladiolus starch has been extensively studied by some authors [10]. So far, there has been no work on the derivatization of starch from this plant.

MATERIALS AND METHODS

Materials

Sodium metabisulphite, sodium hydroxide, sulphuric acid, dimethyl sulphoxide, iodine and copper sulphate (Merck); dextrin (Matheson Coleman & Bell); and cyclohexane, potassium iodide, sodium thosulphate, and glucose (BDH) were used as procured from their local suppliers. All other reagents and solvents were of analargrade and were used without further purification. Distilled water was obtained using a glass still apparatus while gladiolus starch was obtained from a batch processed in our laboratory.

Extraction of gladiolus starch

The fresh corms were weighed, peeled, washed and milled. The resultant paste was extracted with distilled water, strained through a muslin cloth and the starch milk obtained was allowed to sediment under gravity and thereafter, the water was decanted. The sediment starch was then washed several times with clean water until a clean starch was obtained.

Purification of gladiolus starch

The purification followed the procedure earlier described [11]. After the last sedimentation above, the crude starch was soaked in 0.1 N sodium metabisulphite for 24 h. The starch was removed and soaked in 0.1 N sodium hydroxide solutions for 24 h, followed by decanting and washing several times with distilled water. Finally, the starch was soaked in 0.1 N sulphuric acid solutions for 12 h, followed by washing until the final starch suspension was neutral to litmus. The starch was collected, dried at 40°C, milled and stored in an airtight container.

Defatting

The raw starch was dissolved in dimethylsulphoxide, filtered and later precipitated with absolute ethanol just prior to dextrinization [12].

Dextrinization

Gladiolus starch was dextrinized in each case by heating 200 g of the dried starch above in an oven (Gallenkamp, model OV 880, England) without the addition of any other reagent [13, 14], at 120°C, for 5 h and 200°C for 8 h

corresponding to gladiolus starch derived dextrin batch 1 (GSDD1) respectively. At the end of the roasting period, the dextrins were recovered and passed through a 100 mesh to loosen any powder lump.

Identification tests for pyrodextrins

The procedures described in the compendium [15] were adopted. 1 g quantity of GSDD1 or GSDD2 was boiled in 50 ml of water, cooled and 0.05 ml of 0.005 M iodine solution was added to 10 ml of the mixture, and the colour noted. To fresh 5 ml of the mixture above was added 2 ml of 2 M sodium hydroxide solution and 0.5 ml of copper sulphate solution (10% w/v in distilled water) dropwise with shaking and the final solution brought to boiling. The colour of the precipitate produced was noted. Other tests such as microscopy, loss on drying, ash content and pH of 5% w/v solution were carried out as described in the compendium [15].

Solubility determination

A saturated solution of each of the pyrodextrins was prepared by shaking an excess of each in water and allowing the mixture to stand undisturbed for 24 h. The mixture was filtered through a Whatman No. 1 non-adsorbent filter paper to give clear filtrates. 10 ml quantity of each of the pyrodextrin solutions was evaporated to dryness in a pre-weighed dry glass crucible. The weight of the residue corresponding to the solubility was calculated for each batch.

Equilibrium moisture content

1 g quantity of GSDD1 aor GSDD2 was weighted on a blance (KGD 7470, Sauter Germany), and dried to a constant weight at 105°C in a hot air oven. The loss in weight was expressed as per cent loss in weight equivalent to the moisture content of each batch.

Density determination

Bulk and tapped densities

2 g quantity of each of the pyrodextrins was weighed out and transferred into a 10 ml measure. The bulk volume (Bv) occupied was noted. The measure containing the pyrodextrin in each case was tapped on the bench until there was no further reduction in volume (~ 50 times), and the tapped volume (Tv) noted. The bulk density (BD) and the tapped density (TD) of each batch were calculated from Eqs. 1 and 2.

$$BD = \frac{2g}{Bv} \quad \text{.....(1)}$$

$$TD = \frac{2g}{Tv} \quad \text{.....(2)}$$

Carr's compressibility indices and Hausner ratios were further calculated from BD and TD.

True density

The true densities were determined by non-solvent displacement technique. For each batch, 50 ml pycnometer was weighed empty to give a weight W_1. It was filled with cyclohexane and weighed again (W_2). The difference in weights (W_2- W_1) was recorded as W_3. One gram of the pyrodextrin was placed in the empty pycnometer and later filled with cyclohexane and then weighed again (W_4). The true density (It) was obtained from Eq. 3.

$$It\ (g/ml) = \frac{W_3 \times W_2}{25(W_1 + W_2 + W_3 - W_4)} \quad \text{.....(3)}$$

Determination of reducing sugar content

The method described in their compendium was adopted [15]. 2 g quantity of GSDD1 or GSDD2 was mixed with 100 ml of water, diluted to 200 ml with water and filtered. A 20 ml volume of the mixture was mixed with 10 ml of alkaline cupri-tartaric solution, boiled rapidly for 2 min and cooled immediately. 5 ml volume of a 300 g/L solution of potassium iodide and 10 ml of 1 M sulphuric acid solution were added, mixed well, and titrated immediately with 0.1 M sodium thiosulphate solution using starch solution as indicator. The procedure was repeated with 20 ml of a 1 g/L solution of glucose. A blank titration was also carried out and the result recorded.

Effect of concentration on viscosity

Increasing concentrations of GSDD1, GSDD2 and standard dextrin (SDD) were prepared in distilled water to contain 1, 2, 3, 4 and 5% w/v. The solutions were allowed to stand for 24 h and the viscosity readings were thereafter determined in a viscometer (Haake Rotovisko, model RV1) at a speed of 64.8 .rpm (gear 9), and a medium sensor with a constant, K equal to 0.261. Using the average instrument reading (four per concentration), the apparent viscosities (n) of the different concentrations were determined using Eq. 4.

$$n\,(cP) = U.S.K. \quad \ldots\ldots (4)$$

where U is the speed factor and S is the average instrument reading. All measurements were done at room temperature. (25°C).

Surface tension determination

The surface tensions of 2.5% w/v solutions of GSDD1, GSDD2 and SDD were determined with a Lecomte du Nouy tensionmeter (A. Kruss model Nr-3124 Hamburg).

Molecular weight determination by dilute solution viscometry

The molecular weights of GSDD1 and GSDD2 were determined by dilute solution viscometry using Ostwald U-tube viscometer as described by Vasquez et al [16]. Three viscosity grades of SCMC were used as standards. Relative viscosities (n_{rel}) of various concentrations of GSDD1, GSDD2 and SCMC corresponding to 0.1, 0.2, 0.3, 0.4 and 0.5 % w/v respectively were determined in an Ostwald U-tube viscometer. Efflux times of the different concentrations were recorded and their different n_{rel} were calculated from Eq. 5.

$$n_{rel} = \frac{n_p}{n_w} = \frac{l_p t_p}{l_w t_w} \quad \ldots\ldots (5)$$

where l_p and l_w are respectively the densities of the pyrodextrins or SCMC solutions and water, t_p and t_w are their respective mean efflux times while n_p and n_w are respectively the relative viscosities of the pyrodextrins or SCMC solutions and viscosity of water. Average of four efflux times was used in each case and all the determinations were done at 25°C.

From the relative viscosities, the specific viscosities (n_{sp}) for each concentration were calculated using Eq. 6.

$$n_{sp} = n_{rel} - 1 \quad \ldots\ldots (6)$$

Similarly, the corresponding reduced viscosities were obtained from Eq. 7.

$$n_{red} = \frac{n_{sp}}{C} \quad \ldots\ldots (7)$$

where C is the corresponding concentration and n_{red} is the reduced viscosity.

Graphs of n_{sp}/C against C for all the batches were constructed to obtain the intrinsic viscosities [27]. Eq. 8 was then used to obtain the molecular weights of the pyrodextrins while making use of the molecular weights of the three grades of SCMC

$$[n] = KM^a \quad \ldots\ldots (8)$$

where K and a are constants characteristic of a particular polymer-solvent system, M is the mean viscosity molecular weight.

RESULTS AND DISCUSSION

Microscopically, the pyrodextrins granular structures resembled those of the starches from which they were manufactured. However, there were prominent cleftular openings. These cleftular openings may be responsible for the water solubility of the pyrodextrins. The photomicrographs are shown in Fig. 1. The opening was found to be greater in GSDD2 than in GSDD1. This may be because of the greater heating temperature and longer dextrinization time. The energy required to break the starch-to-starch secondary bonds depends on the closeness of molecular packing and the degree of association. The greater the degree of association, the greater the energy required to separate the molecules and the greater their resistance to heat. Higher energy provided at higher temperature would thus produce greater effect on the clefts.

All the batches of pyrodextrins conformed to the standards stated in the official compendium [15]. The two pyrodextrins including the standard dextrin gave purple colour required by the test. This result showed that there was actual hydrolysis of the chain length of starch to yield starch oligosaccharides. It has been documented that dry roasting of starch completely hydrolyses starch and such heat-treated starches contain appreciable quantities of maltose detectable by means of Fehling's solution in comparison with partially dilute acid-treated hydrolysed starches [17]. The results of some miscellaneous tests (loss on drying, ash value, and pH of a 5% w/v solution in carbon dioxide free water) are presented in Table 1. All the results also conformed to the pharmacopoeial standard attesting further to the high quality of the pyrodextrins produced.

The solubility of the pyrodextrins as presented in Table 1 indicated that they belong to the category referred to as "very soluble" in the Bristish Pharmacopoeia [18]. The pyrodextrins were insoluble in organic solvents and dissolved very fast in boiling water. The aqueous solubility of these pyrodextrins may be as a result of the opening of the clefts by the action of heat and also

due to the formation of starch oligomers of greater aqueous solubility. GSDD1 was found to be more soluble than GSDD2. When starch is heated, a complex combination of hydrolysis, rearrangement and repolymerization occur to give pyrodextrins and in the process, some branchings are introduced and there may be reduction in molecular size [2, 19]. Branching of polymers reduces their solubility. GSDD1 may have contained less branch points. This result corroborates with the result of the molecular weight determination GSDD1 had higher molecular weight than GSDD2 (Table 1). Longer dextrinization of GSDD2 may have resulted in lower molecular weight starch oligomers compared with GSDD1. Figs 2 and 3 show the plot of reduced viscosity against polymer concentration where intrinsic viscosities were extrapolated while Fig. 4 shows the SCMC calibration plot from where 'K' and 'a' in Eqn. 8 were calculated. In all, there was a reduction in molecular weight compared to that of the raw gladiolus starch determined by the same method [10]. Also, the higher solubility of GSDD1 may be as a result of the higher reducing sugar content than in GSDD2 (Table 1). This result also confirms the greater degree of branching in GSDD2 than in GSDD1, in that there were more free reducing sugars available for interaction with the reagents than in GSDD2.

The surface tensions (of 2.5% w/v solution in water) of the pyrodextrins are presented in Table 1. There was a reduction in the surface tension of water. This test was carried out to ascertain the ability of the pyrodextrins solutions to wet pharmaceutical powders during granulation with water. The lowering of the surface tension of water by the pyrodextrins implied that they can effect faster wetting of pharmaceutical powders. Solutions of these pyrodextrins may thus be appropriate for granulating hydrophobic pharmaceutical powder mixtures. They can easily form strong solid bridges in-between particles of powder mix for granulation.

The equilibrium moisture contents of the pyrodextrins (Table 1) were higher than the reported value of 5% determined by Karl technique [4]. This may be as a result of the difference in method of determination. GSDD1 had a moisture content of 11.26% while GSDD2 had a moisture content of 6.60%. Except when used as binders in wet granulations, these pyrodextrins may not be useful in the production of tablets where active ingredient responds severely to moisture and also in order to maintain tablet integrity. This property may limit their possible use as directly compressible materials. However, compressible materials are required to possess a limiting amount of moisture that has been found to aid bonding in powders or granules. It is also known that it is the unbound rather than the bound water content of a material that is important as far as chemical stability is concerned, since the solid-like and bound portions do not induce hydrolysis [20, 21]. The suitability of these pyrodextrins in the formulation of hydrolysable drugs such as aspirin cannot be made from these results since the various states of the moisture have not been investigated.

The pyrodextrins had high bulk and tapped densities (Table 1) comparable to reported values for dextrins [4]. Their true densities were almost equal to that of the parent starch (1.53 g/ml). These pyrodextrins may be good candidates for direct compression tabletting because of their high bulk densities [22]. Also these phyrodextrins had low values of Carr's compressibility indices suggesting good compacts at low compaction pressures. Carr's compressibility indices and Hausner ratios gave an idea on the rate of consolidation of powders and the compression pressure dependent nature of a material. High values suggest high resistance to fast consolidation during die filling and actual compression.

The result of the effect of concentration on viscosity at 25°C is presented in Fig. 5. There was almost a linear increase in viscosity with increase in pyrodextrin concentration. This is in consonance with most polymers. However, for the pyrodextrins, the average viscosity at each concentration is low. this is true because dextrins are known to form low vicosity pasters with greater stablity in water than starches [2], hence, the name thin-boiling starches. The viscosities generated however, will be enough to suspend any pharmaceutical insoluble powder of appropriate size and also allow pourability from a container. The viscosities will not impede any mixing process

during granulation.

Conclusion

Pharmaceutical excipient with multfunctionality can be produced by roasting of gladiolus starch for different length of time at different temperatures. The performance of the pyrodextrins could be adjusted by the adjusting the roasting time at each temperature or vice versa.

Acknowledgement

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Table 1. Results of the parameters evaluated

Parameter	Magnitude	
	GSDD1	GSDD2
Loss on drying (%)	7.1	5.1
Ash value (%)	0.38	0.44
pH of 5% solution	6.5	6.8
Solubility (g/100 ml)	8.64	7.30
Surface tension (Nm^{-1})	67.6	65.0
Bulk density (g/cm^3)	0.712	0.721
Tapped density (g/cm^{-3})	0.833	0.870
True density (g/cm^3)	1.5319	1.5320
Moisture content (%)	11.26	6.60
Intergranular porosity	0.5352	0.5353
Carr's compressibility index (%)	14.53	18.16
Hausner ratio	1.170	1.222
Average viscosity molecular weight	184,086.72	114,992.77
Reducing sugar content (%)	0.33	0.20

Legends to the Figures

Fig. 1. Photomicrographs of the dextrins (x200)

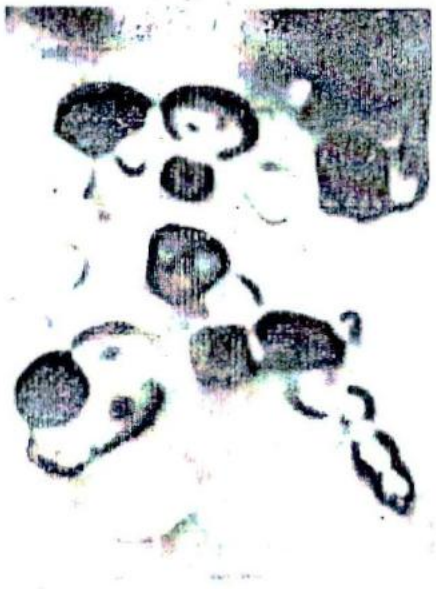
Fig. 2. Plot of reduced viscosity against pyrodextrin concentration
0 - GSDD1; □- GSDD2

Fig. 3. Plot of reduced viscosity against SCMC concentration
x - Low viscosity grade SCMC
●- Medium viscosity SCMC
o- High viscosity SCMC

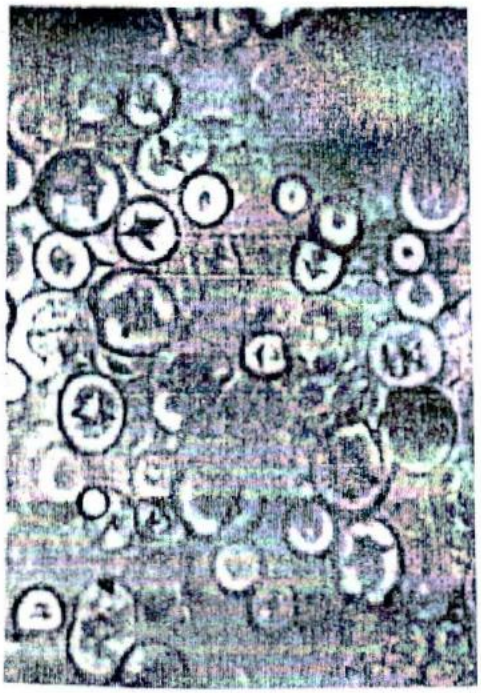
Fig. 4. Calibration plot for SCMC

Fig. 5. Effect of concentration on viscosity at 25°C.
△- GSDD1 O- GSDD2 x- standard dextrin

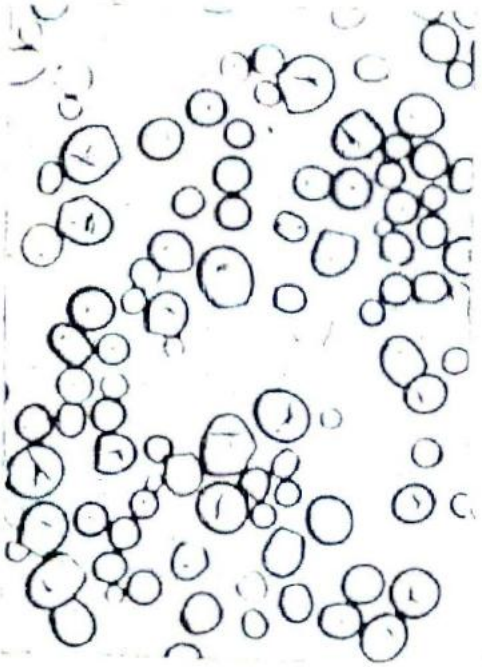
GSDD1



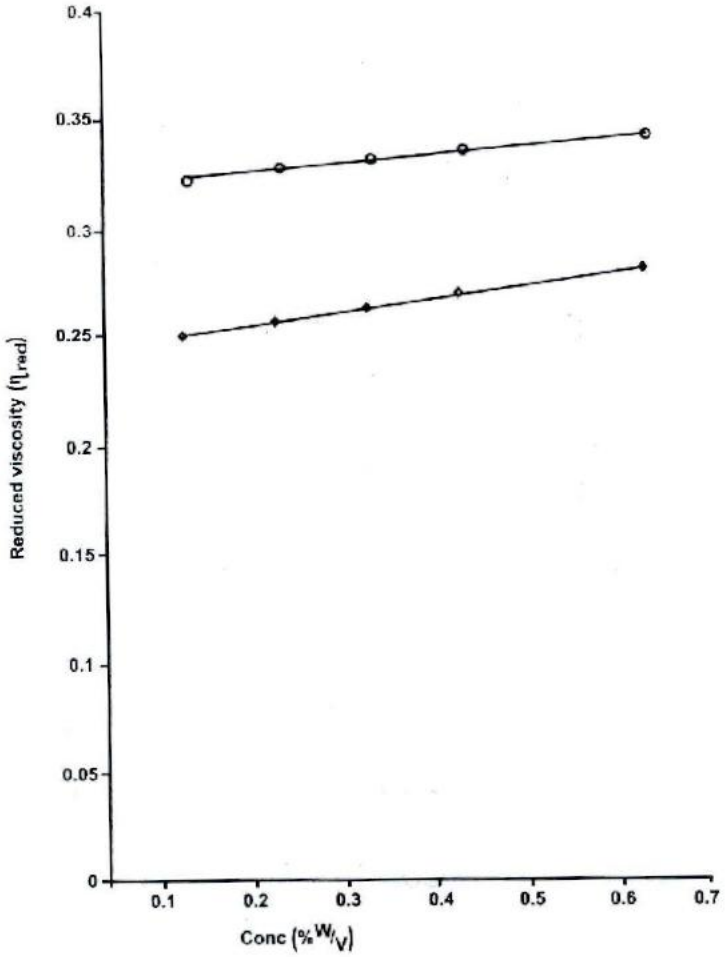
GSDD2

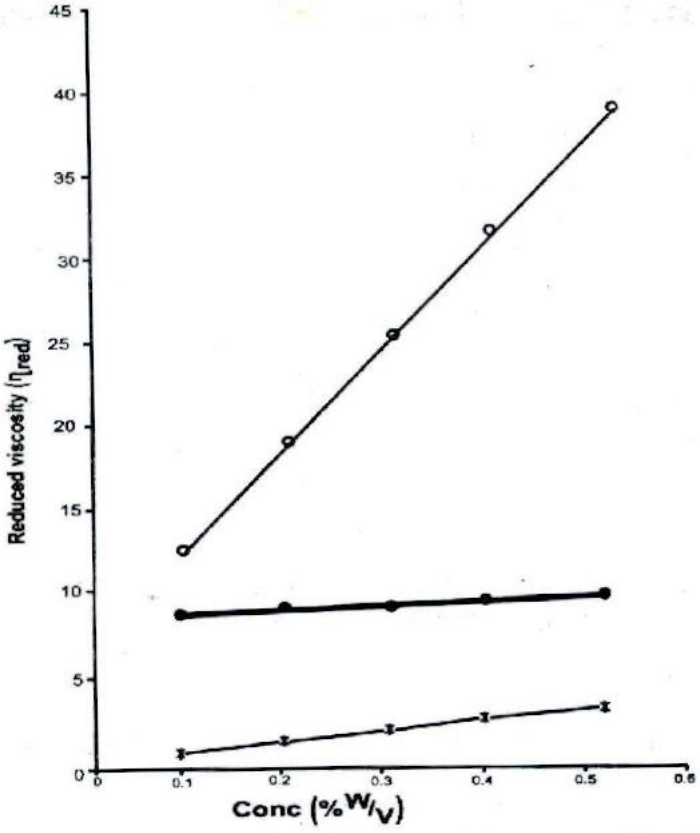


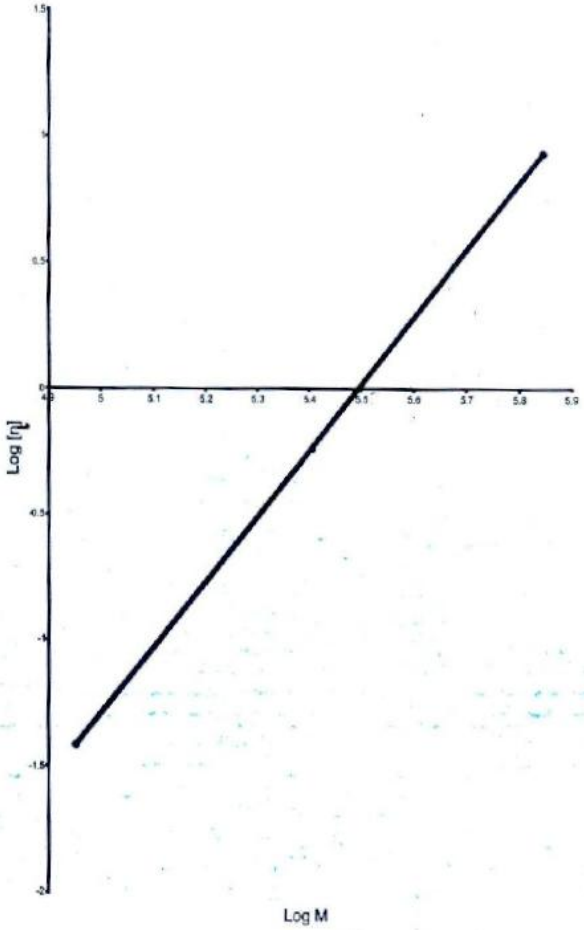
Standard dextrin

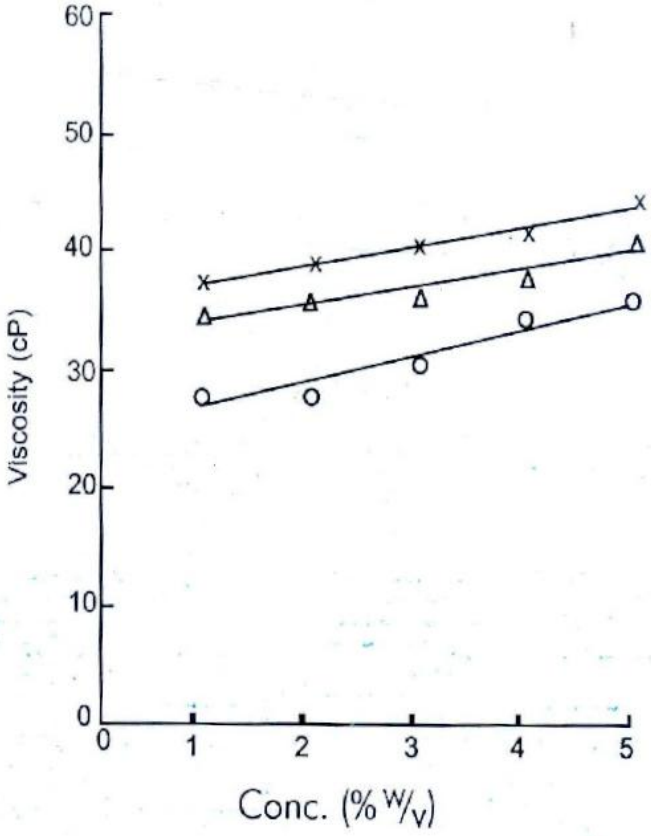


Raw gladiolus starch


0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Reduced viscosity (η_{red})
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Conc (%W/V)


45
40
35
30
25
20
15
10
5
0
Reduced viscosity (η_{red})
0
0.1
0.2
0.3
0.4
0.5
0.6
Conc (%W/V)





REFERENCES

1. Whistler R. L., Smart, C. L. Polysaccharide Chemistry. Academic Press Inc., New York 1953.
2. Saunders K. J. Organic Polymer Chemistry. 2nd edn., Chapman Hall, London, 1988, pp. 312-315.
3. Gliksman M. Gum Technology in Food Industry. Academic Press Inc., New York, 1976, pp. 274-333.
4. Wade A. Weller P. J. Handbook of Pharmaceutical Excipients, 2nd edn., The Pharmaceutical Press, London, 1994.
5. Mollan H. J., Celik M. The effect of lubrication on compaction and post-compaction properties of directly compressible maltodextrins. Int. J. Pharm. 1996; 144: 1-9.
6. Parrot E. Comparative evaluation of a new direct compression excipent, soludex. Drug Dev. Ind. Pharm. 1989; 15 : 561-583.
7. Papadimitriou E., Efentakis M., Choulis N. Evaluation of maltodextrins as excipients for direct compression tablets and their influence on the rate of dissolution. Int. J. Pharm. 1992; 86: 131-136.
8. Mollan M. J. Celik M. The effect of humidity and storage time on the behaviour of maltodextrins for direct compression. Int. J. Pharm. 1995; 114 : 23-32.
9. Mollan M. J., Celik M. Characterization of directly compressible maltodextrins manufactured by three different processes. Drug Dev. Ind. Pharm. 1993; 19:2335-2358.
10. Adikwu M. U., Onyia C. C., Ofokansi, K. C. Evaluation of the physicochemical properties of Gladiolus actinomorphanthus starch. Acta Pharm. 1997; 47 : 197-202.
11. Attama A. A., Adikwu M. U. The physicochemical properties of starch derived from Tacca involucrata. Nig. J. Nat. Prod. & Med. 1999; 3 : 70-72.
12. Knutson C. A. A simplified colorimetric procedure for determination of amylose in maize starch. Cereal Chem. 1986; 63 : 89 - 92.
13. Budavari S. The Merck Index, 11th edn., Merch & Co., Inc., NJ, 1989, p. 465.
14. Bauer K. H., Lehmann K., Osterwald H. P., Rothgang G. Coasted Pharmaceutical Dosage Forms. CRC Press, Boston, 1998, pp. 251-252.
15. European Pharmacopoeia, 3rd edn., Council of Europe, Strasbourg, Supplement 2001, pp. 1097-1098.
16. Vasquez M. J. Casaldeney M., Dura R, Gomez - Amoza J. L., Martinez-Pacheco R., Souto C., Concehiro A. Atenolol release from hydrophilic matrix tablets with HPMC mixtures as gelling agents; effect of the viscosity of the HPMC mixture. Eur. J. Pharm. Sci. 1996; 4 : 39 - 48.
17. Schmidt P. C., Tabletting characteristics of sorbitol. Pharm. Technol. 1983; 7 : 65 - 74.
18. British Pharmacopoeia. Vol. 1, Her Majesty's Stationary Office, London, 1988.
19. French D. Chemical and physical properties of starch. J. Animal Sci. 1973; 37: 1048-1061.
20. Lund W. The Pharmaceutical Codex. Principles and Practice of Pharmaceutics. 12th edn., The Pharmaceutical Press, London, 1994, pp. 277-310.
21. Zografi G., Yang A.Y.S., Brenner G.S., Kontny M. J. Surface area and water vapour sorption of microcrystalline cellulose. Int. J. Pharm. 1984; 18:99-116.
22. Armstrong N. A Selection of excipients for direct compression tablet formulations. Pharm. Technol. Eur. 1998; 39:24-30.