Research Article

Evaluation of Native and Carboxymethyl Yam (*Dioscorea esculenta*) Starches as Tablet Disintegrants

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Abstract

Native yam starch and carboxymethyl yam starch (CMS) were evaluated as tablet disintegrants in comparison with various starches i.e., corn starch, tapioca starch and rice starch. Direct compression composition comprised dibasic calcium phosphate as a filler, each starch at various concentrations between 3-15% w/w as a disintegrant and magnesium stearate as a lubricant. Hydrochlorothiazide (HCTZ) was used as a model drug for drug dissolution testing. Tablet properties including hardness, friability, disintegration and dissolution were evaluated. The results showed that tablet hardness increased with the amount of starch in the tablets. Tablets containing yam starch and rice starch showed higher tablet hardness than other native starches, while the tablets containing CMS showed obvious superior hardness to that of the other starches. The disintegration of tablets containing native yam starch was faster than that of tablets with corn, rice, and tapioca starches. With increasing native starch concentrations, the disintegration of the tablets was found to be faster. Tablets with CMS disintegrated in a similar manner to those with native yam starch when the concentrations were up to 9% by weight. The disintegration was delayed with higher concentrations. The HCTZ tablet with yam starch as a disintegrant gave faster initial dissolution than the others. It can be concluded that native yam starch and its carboxymethyl derivative can be used as superior disintegrants in tablet formulation.

Key Words: Yam starch; Carboxymethyl yam starch; Disintegrant; *Dioscorea esculenta*

Introduction

A disintegrant is a substance added into a tablet blend to facilitate the breakup of the tablet contents into smaller particles. This will promote a more rapid release and subsequent absorption of the active drug. A good disintegrant must be effective at low concentrations to avoid or reduce the influence on the tablet properties such as hardness, friability or compressibility. Starches i.e. corn, potato, and wheat starch were the first disintegrating agents used in tablets (Bandelin, 1989; Ingram and Lowenthal, 1966; Kerf et al., 2001; Orelli and Leuenberger; 2004). Moreover, native starches have been modified to obtain various desired properties. Carboxymethyl starch is a starch derivative in which the hydroxyl groups in anhydroglucose unit were etherified with carboxymethyl groups. The degree of substitution (DS), the average number of carboxymethyl groups per anhydroglucose unit, markedly affects the properties of the starch (Stojanovic et al., 2005). The CMS made from potato starch has been used for pharmaceutical preparations, as a super disintegrant (Arthur and Kibbe, 2000).

The Yam (*Dioscorea sp.*) is a local plant of many countries, i.e., Nigeria, Jamica, Brazil, China, and Thailand (Riley et al., 2004; Alves et al., 2002; Shujun et al., 2006; Yu et al., 1999). Yam starch, which was obtained from the yam tuber, has been studied as an alternative source for the food industry (Alves et al., 2002; Brunnschweiler et al., 2005; Freitas et al, 2004). The most common yam found in Thailand is *Dioscorea esculenta* (Lour.) Burk. (lesser yam) (Vorasuntharosoj, 2001). Its starch has not been used in the food industry and no studies of its pharmaceutical application have been reported. In a preliminary study (Kawrueng, 2005), the gelatinization temperature of 78.0 ˚C was observed and its swelling power was higher than cassava starch.

This study was designed to evaluate the efficacy of yam starch (*D. esculenta*) and its carboxymethyl derivative as tablet disintegrants compared with other commercial native starches.

Materials and Methods

Materials

Hydrochlorothiazide (HCTZ; China Chemical, China), dibasic calcium phosphate (Emcompress®, Chemische Farbrik Budenheim, Germany) and magnesium stearate (Faci Asia Pacific Pte LTD., China) were used as the active drug, filler and lubricant, respectively. Disintegrants in this study were corn starch (Meelunie, Holland), tapioca starch (National Starch & Chemical, Thailand), rice starch (Erawan Pharmaceutical Research and Laboratory Co., LTD, Thailand) and yam starch (*D. esculenta*), which was harvested in November (harvest season), was purchased from a local market in Nakornpathom.

Extraction of yam starch

Yam tubers were washed, peeled and trimmed to remove defective parts. The tubers were then sliced, diced and blended with distilled water in a food blender. The mixture was sieved through a 80-mesh sieve and the retained solids were exhaustively rinsed on the sieve with distilled water. The filtrate was allowed to stand overnight at 15 ˚C, then the precipitate was collected. The re-suspension and sedimentation operations were repeated until white product was obtained. The product was dried at 50 ˚C for 6 hours. The yam flour, which its properties met the requirement of starch in The United State Pharmacopoeia (USP 27/ NF 22, 2004) was used in this study. The percentages of extracted yam starch were collected.

Carboxymethyl yam starch

Native yam starch (10.0 g) was suspended in water (100 mL). An aqueous 3M sodium hydroxide solution (200 mL) was added. The mixture was stirred at room temperature for 10 minutes. Sodium monochloroacetate (10.0 g) was added and stirring was continued for 2 hours. The pH of the mixture was adjusted to about 5.0 by addition of 50% glacial acetic acid. The carboxymethyl starch was filtered and washed with aqueous ethanol. The modified starch was dried at 50 ˚C for 6 hours. The dried carboxymethyl starch was passed through a 100 mesh

sieve. The degree of substitution was determined using a back titration method as reported by Stojanovic et al., (2005).

Morphology

The shape and surface structure of native yam starch and CMS were studied using scanning electron microscopy (Camscan analytical, Maxim 2000s, UK). The starch sample was attached on a stub and coated with gold to increase its conductance. The sample was viewed and photographed.

Swelling power

The swelling power (by weight) of starches was measured using the method modified from Abera and Rakshit (2003). Starch (0.5 g) was dispersed in water (10 mL). The suspension was heated at 85 °C in a water bath for 30 minutes with vigorous shaking every 5 minutes. The starch gel was then centrifuged at 2,200 rpm for 15 minutes. The weight of sediment was used for calculation of the swelling power. The determination was run in triplicate.

Amylose content

The amylose content of the starch was determined using chemical reaction between amylose and iodine. Starch (0.5 g) was dispersed in water (100 mL). The suspension was heated at 85 °C in a water bath for 30 minutes with vigorous shaking every 5 minutes. The slurry was then filtered. Iodine solution 0.1 mL was added to 0.5 mL of the filtrate and purified water was used to adjusted volume to 10 mL. After mixing, absorbance was read at 590 nm using a UV/Visible spectrophotometer (Hitachi, U2000, Japan).

Tablet preparation

The efficiency of yam starch as a tablet disintegrant was evaluated and compared with tapioca starch, corn starch rice starch and carboxymethyl yam starch. Dibasic calcium phosphate and magnesium stearate were used as filler and lubricant, respectively. HCTZ was used as a model drug in drug release evaluation. The formulations are shown in Table 1. Tablets were prepared using the direct compression method. All ingredients except magnesium stearate were mixed for 15 minutes. After that magnesium stearate was added and further mixed for 5 minutes. The powder blend was compressed into tablets using a hydraulic compressor (Riken Power, P-16B-027, China) equipped with a 8-mm flat face punch. The tablet was compressed at a controlled compression pressure of 150 MPa. The tablet weight was 250 mg.

Table 1 Tablet formulations.

Ingredient	Blank tablet (%w/w)	HCTZ tablet (%w/w)
Starch as disintegrant	0,3,6,9,12,15	9
HCTZ	-	20
Magnesium stearate	0.25	0.25
Emcompress® q.s. to	100	100

Tablet hardness

The tablet hardness was determined on an electronic digital hardness tester (Erweka, TBH2PTD, Germany). Ten tablets were measured individually. The mean values and standard deviation were calculated.

Tablet friability

The friability was conducted on twenty tablets using a friability tester (Erweka, TA200, Germany). The drum was rotated at 25 rpm for 4 minutes. Loss of tablet weight with respect to the initial value was then calculated as percent friability.

Disintegration time

The disintegration time was determined according to the disintegration test for uncoated tablets of The United State Pharmacopoeia (USP 27/ NF 22, 2004). Disintegration apparatus (Vankel, VK100, USA) was employed. Six tablets were tested. One tablet was placed in each of the six tubes of the basket and operated of the apparatus. Distilled water was maintained at 37±2 °C as the immersion fluid. The average disintegration time and standard deviation of six tablets were determined.

Dissolution test

The dissolution test of hydrochlorothiazide tablet followed the monograph of HCTZ tablets in The

United States Pharmacopoeia (USP 27/ NF 22, 2004). The dissolution apparatus setup consisted of a dissolution station using rotation baskets (Vankel, VK700, USA) and an ultraviolet (UV)/visible spectrophotometer (Hitachi, U2000, Japan). The test was conducted in the dissolution flask containing 900 mL of 0.1N hydrochloric acid for 60 minutes. The absorbance was read at the wavelength of 272 nm every 10 minutes. The amount of drug release from the tablet at specified times were determined as percent of labeled amount.

Results and Discussions

Extraction of yam starch and preparation of carboxymethyl yam starch

Wet yam tuber contained about 10% yam starch. The properties of obtained yam starch were met the requirements of starch specified in The United States Pharmacopoeia (USP27/NF22). Carboxymethylation of yam starch in aqueous medium at room temperature for 2 hours yielded CMS with a degree of substitution of 0.14.

Properties of yam starch and CMS

Scanning electron microphotographs of yam starch and CMS shown in Figure 1 indicated that the yam starch granules were polygonal with particle size of 2-10 μm. Eruption of starch granules resulted in porous particles being observed in scanning electron micrographs of carboxymethyl yam starch (CMS).

Swelling power

The swelling power of the starches is presented in Table 2. The decreasing order of the swelling power was CMS > yam starch > tapioca starch > corn starch > rice starch. Tester et al., (2004) suggested that swelling power of starch was attributed to amylopectin, the swelling power has a negative correlation with amylose. According to the amylose content of yam, rice, corn, and tapioca starches shown in Table 2, rice and corn starch (cereal seed starch) have higher amylose than yam and tapioca starch (tuberous starch). For CMS, the swelling power was much higher than that of the native yam starch. More water can penetrate into the starch granules due to the hydrophilicity of the

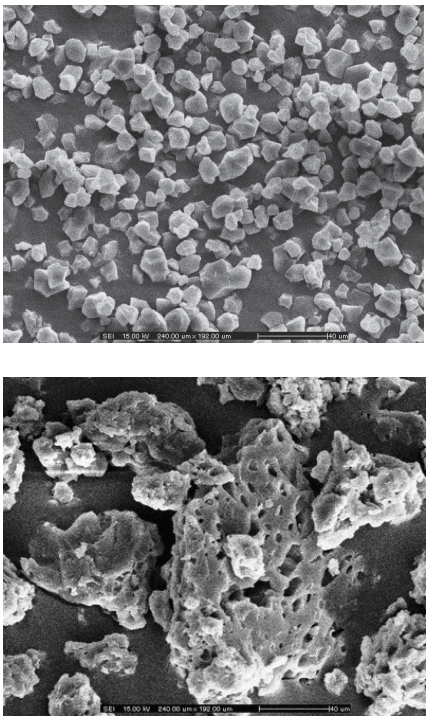

Figure 1 Scanning Electron Micrograph of yam starch scale bar = 40 μm (a) Native yam starch, (b) Carboxymethyl yam starch.

Table 2 Swelling power and amylose content of starches.

Starch	Swelling power, Times (SD)	Amylose content, % (SD)
Rice starch	9.32 (0.12)	27.22 (0.24)
Corn starch	10.37 (1.24)	22.61 (0.22)
Tapioca starch	15.54 (1.52)	19.71 (0.70)
Yam starch	17.04 (0.74)	12.24 (0.30)
CMS	63.34 (0.81)	2.32 (0.02)

carboxymethyl groups (Wurzburg, 1986) resulted in swelling of the starch granule and dissolution in water. The amylose content of CMS was decreased as a resulted of the destruction of the helical structure during carboxymethylation. Therefore, the concentration of amylose-Iodine complex was lower, resulted in the amylose content.

Tablet evaluation

Hardness The effect of concentration of the yam starches compared with tapioca starch, corn starch and rice starch on tablet hardness is shown in Figure 2. The hardness increased with the concentration of starch in all formulations. The hardness of a tablet is a parameter that describes the amount and the strength of bonding in the tablet. From this study, the tablet containing CMS showed a superlative degree of hardness. Since CMS is more polarity than native starch, the particles were bound with more amount and stronger hydrogen bonds. Such the CMS that has polar surface, at equilibrium under normal conditions, it had a water sorption layer which might possibly interact over a high concentration of hydrogen bonds. The two particles have a joint water sorption layer resulting in a strong interparticular attraction (Fuhrer, 1996). Thus, the boding strength of tablet containing CMS was higher than the native starch. Yam starch and rice starch, which have polygonal shape, gave higher tablet hardness than corn and tapioca starches (which have nearly round shape (Arthur and Kibbe, 2000; Thiengthirathum, 1995)). The polygonal shape of yam and rice starches possessed higher degree of particle inter-locking during rearrangement phase of compression that enhanced particle consolidation during compression.

Friability The tablet friability decreased with increasing amount of starch in the tablet starch concentration (shown in Figure 3). The higher the tablet hardness, the lower tablet friability was observed, because the interparticulate cohesiveness increased with increasing starch concentration. The increasing order of tablet friability was CMS < yam starch < rice starch < corn starch < tapioca starch, respectively.

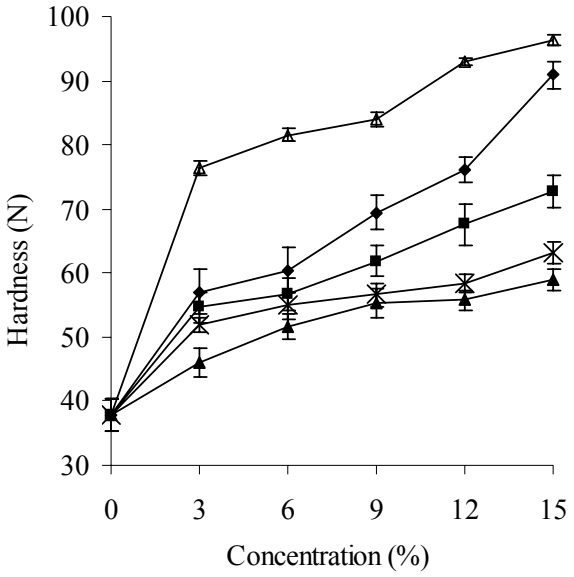

Figure 2 Effect of starch concentrations on the crushing strength of tablets. (■=Rice starch, ▲=Corn starch, ×=Tapioca starch, ◆=Yam starch, △=Carboxymethyl yam starch)

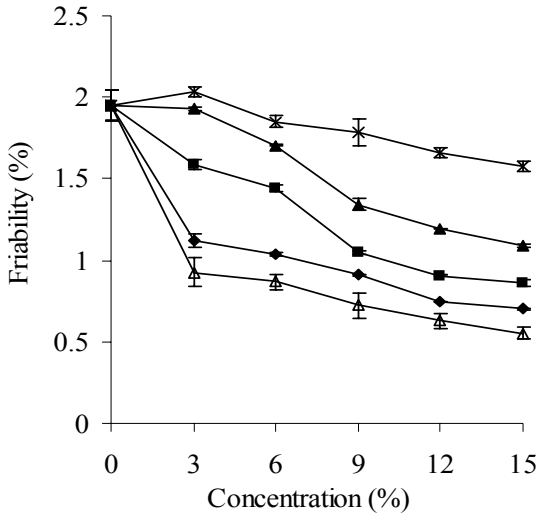

Figure 3 Effect of starch concentrations on the friability of tablets. (■=Rice starch, ▲=Corn starch, ×=Tapioca starch, ◆=Yam starch, △=Carboxymethyl yam starch)

Disintegration time The effect of starch concentration on the disintegration time of the tablets is showed in Figure 4. The tablets without starch and the tablets with 3% of rice starch, corn starch, or tapioca starch were not disintegrated in the tested time of 30 minutes, but tablet containing 3% of yam starch and CMS disintegrated at 3 and 11 minutes, respectively. Tablet containing a native starch that has higher swelling power disintegrated faster. At increasing amount of all native starches, a decrease in the disintegration time was seen. This result indicated that the increasing in swelling force by increasing amount of starch had more pronounce effect on the disintegration time than did the increased tablet hardness. Swelling is a predominant one of the disintegration mechanism (Marshall and Rudnic, 1990; Hill, 2006). The tablet formulated with CMS disintegrated more slowly than the tablet with native starches, especially in high concentrations of 12% and 15% by weight. This result was related to the swelling characteristic of CMS. Viscous or gel mass was observed when CMS was suspended in water at high concentrations. The viscous gel mass formation could impede the penetration of water in to the tablets and retarded the disintegration. The use of CMS as a tablet disintegrant in this study seemed to have the optimum concentration at 9% by weight.

Dissolution The dissolution profiles of HCTZ tablets are shown in Figure 5. It can be seen that the dissolution corresponded to the disintegration property of the tablets. The faster tablet disintegration resulted in a faster drug release. However, all formulations were released more than 80% in 40 minutes, and a complete dissolution was obtained in 60 minutes.

Conclusions

Yam starch and CMS were evaluated for theirs efficacy as tablet disintegrants in comparison with corn starch, rice starch and tapioca starch. The results revealed that the shape of yam starch granules were polygonal with a size range of 2-20 μm. Its polygonal shape played a major role in increasing tablet

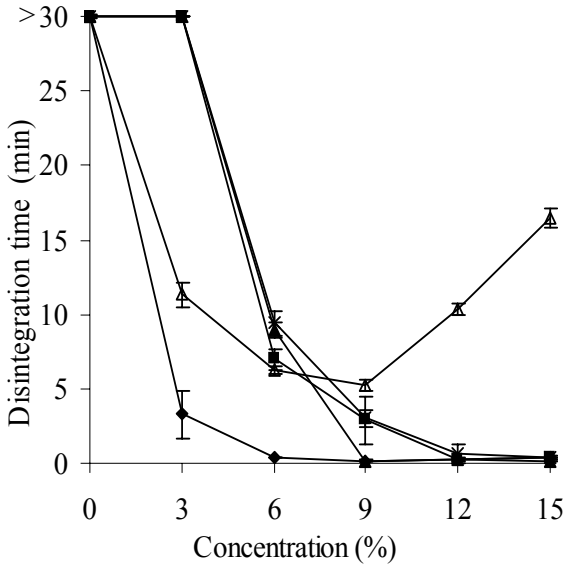

Figure 4 Effect of starch concentrations on disintegration time of tablets. (■=Rice starch, ▲=Corn starch, ×=Tapioca starch, ◆=Yam starch, △=Carboxymethyl yam starch)

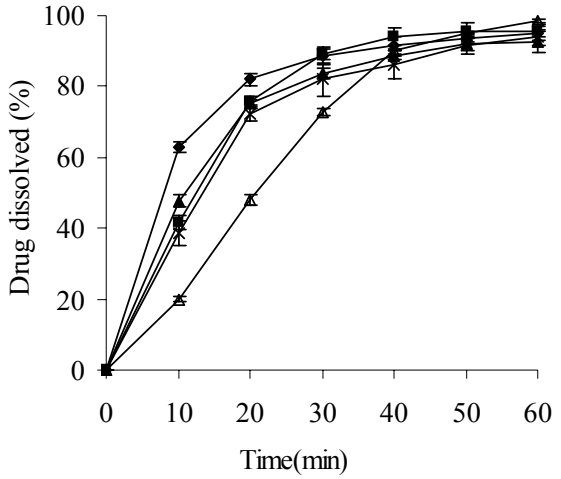

Figure 5 Effect of starch on drug release from tablet. (■=Rice starch, ▲=Corn starch, ×=Tapioca starch, ◆=Yam starch, △=Carboxymethyl yam starch)

hardness. Moreover, the tablet containing yam starch showed the fastest disintegration time, especially at low concentrations. The highest swelling power of yam starch has a marked effect on the tablet disintegration. CMS showed higher swelling power and more viscous gel. It could also be used as a tablet disintegrant. However, at high concentrations, the tablet disintegration and dissolution were retarded due to formation of gel mass. With this special property, CMS had a potential to be used in drug controlled release dosage forms.

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References

Abera, S. and Rakshit, S. K. (2003) Comparison of physicochemical and functional properties of cassava starch extracted from fresh root and dry chips. *Starch* 55: 287-296.

Alves, R. M., Grossmann V. M., Ferrero, C., Zaritzky, N. E., Martino, M. N., and Sierakoski, M. R. (2002) Chemical and functional characterization of products obtained from yam tubers. *Starch* 54: 476-481.

Arthur, H. and Kibbe. (2000) *Handbook of Pharmaceutical Excipients*, 4thed. American Pharmaceutical Association, Washington D.C.

Bandelin, F. J. (1989) Compressed tablets. In *Pharmaceutical Dosage Forms: Tablets* (Liberman, H. A., Lachman, L., Schwartz, J.B., eds.), vol.1, pp.173-177. Marcel Dekker, New York.

Brunnschweiler, J., Luethi, D., Handschin, S., Farah, Z., Escher, F., and Conde-Petit, B. (2005) Isolation, physicochemical characterization and application of yam (*Dioscorea spp.*) starch as thickening and gelling agent. *Starch* 57: 107-117.

Freitas, R. A., Paula, R. C., Feitosa, J. P. A., Rocha,S., and Sierakowski, M. R. (2004) Amylose contents, rheological properties and gelatinization kinetics of yam (*Dioscorea alata*) and cassava (*Manihot utilissima*) starches. *Carbohydrate Polymers* 55: 3-8.

Fuhrer, C. (1996) Interparticulate bonding characteristics of pharmaceutical compacts. In *Pharmaceutical Powder Compaction Technology* (Alderborn, G., and Nystrom, C., eds.) pp.1-15. Marcel Dekker, Inc., New York.

Hill, P. M. (2006) Effect of compression force and corn starch on tablet disintegration time. *Journal of Pharmaceutical Sciences* 65(11): 1694-1697.

Ingram, J. T. and Lowenthal, W. (1966) Mechanism of action of starches as a tablet disintegrant I: factor affect the swelling of starch grains at 37 °C. *Journal of Pharmaceutical Sciences* 55: 614-617.

Kawrueng, P. (2005) Physico-chemical properties of yam (*Dioscorea esculenta*) starch. *Chemistry Senior Project Report*. Faculty of Sciences, Silpakorn University.

Kerf, M. D., Mondelaers, W., Lahorte, P., Vervaet, C., and Remon, J. P. (2001) Characterization and disintegration properties of irradiated starch. *International Journal of Pharmaceutics* 22: 69-76.

Marshall, K., and Rudnic, E.M. (1990) Tablet dosage forms. In *Modern Pharmaceutics* (Banker, G.S., and Rhodes, C.T., eds.) pp.355-471. Marcel Dekker, Inc., New York.

Orelli, J. V. and Leuenberger, H. (2004) Search for technological reasons to develop a capsule or tablet formulation with respect to wettability and dissolution. *International Journal of Pharmaceutics* 287: 135-145.

Riley, C. K., Wheatley, A. O., Hassanc, I., Ahmad M. H., Morrisona, E. Y. A., and Asemota, H. N. (2004) In vitro digestibility of raw starches extracted from five yam (*Dioscorea spp*.)

species growth in Jamaica. *Starch* 56: 69-73.

Shujun, W., Hongyan, L., Wenyuan, G., Haixia, C., Jiugao, Y., and Peigen, X. (2006) Characterization of new starched separated from different chinese yam (*Dioscorea opposite* Thumb.) cultivars. *Food Chemistry* 99(1): 30-37.

Stojanovic, Z, Jeremic, K., Javanovic, S., and Lechner, M. D. (2005) A comparison of some methods for the determination of the degree of substitution of carboxymethyl starch. *Starch* 57: 79-83.

Tester, R. F., Karkalas, J., and Qi, X. (2004) Starch-composition, fine structure and architecture (Review). *Journal of Cereal Science* 39: 151-165.

Thiengthirathum, S. (1995) Tablet disintegration properties of modified tapioca starch. *M.S. Thesis in Pharmacy*. Faculty of Graduate Studies, Mahidol University.

USP 27/ NF 22 (2004) *The United States Pharmacopoeia 27/ The National Formulary 22*, The United States Pharmacopoeial Convention Inc., Asian edition, Port City Press, Baltimore.

Vorasuntharosoj, P. (2001) *Plant Resources of South East Asia: PROSEA*, Sahamit Printing, Bangkok.

Wurzburg, O.B. (1986) *Modified Starches: Properties and Uses*. CRC Press, Inc., Florida.

Yu, B., Fujii, S., and Kishihara, S. (1999) Physicochemical property of huaishan (*Rhizama Dioscorea*) and matai (*Eleocharis dulcis*) starches. *Starch* 51: 5-10.