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Characterization of Apricot Gum as a Binder in Tablet Formulations

Kayısı Zamkının Tabletlerde Bağlayıcı Olarak Kullanılması

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Abstract

In this study, apricot gum (APG) obtained from *Prunus armeniaca* was evaluated as a tablet binder for wet granulation method. Tenoxicam (TNX) was chosen as the model drug. Binding property of APG was compared with other binding agents as gum arabic (GA) and polyvinyl pyrrolidone (PVP). The effect of different compression pressures on the properties of tablets was also investigated. Results indicated APG as a potential pharmaceutical binding agent when compared to GA and PVP.

Keywords: *Prunus armeniaca*; apricot gum; wet granulation; tablet binder; tenoxic

Introduction

Gums are important products used in various fields of industry such as textile, paper, food, cosmetics and pharmaceuticals. They are natural hydrocolloids of fertile properties and of low cost (Huber, *et al.*, 1966). Plant gums are widely used in diverse applications for the formulation of pharmaceutical dosage forms. The major application of gums is in tablets as binding agent (Odeku, and Itiola, 2002; Verma, and Razdan, 2002).

Prunus armeniaca (Apricot) currently cultivated in Turkey is a Prunoidae plant growing in all of the Mediterranean area. Apricot gum (APG) obtained from the incised trunk of the tree contains highly branched polysaccharides mainly consisting of L-arabinose and D-galactose. It has been reported that APG, due to its arabinogalactan structure is used as emulsifying and suspending agents as well (Nurmukhamedov, 1956; Umanskii, 1943).

The aim of this study was to investigate the binding properties of APG in tablets prepared by wet granulation method. APG was compared with other binding agents as gum arabic (GA) and polyvinyl pyrrolidone (PVP). The effects of different compression forces (1000, 1500 and 2000 psi) on the properties of tablets were also investigated.

Experimental

Materials

APG was obtained from *Prunus armeniaca* and purified in our laboratory. Tenoxicam was obtained from Eczacıbaşı Pharmaceuticals Inc. (Turkey), gum arabic and magnesium stearate

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from Merck (Germany), polyvinyl pyrrolidone K-25 from ISP (USA), anhydrous lactose from Borculo Domo (The Netherlands). All other chemicals were of analytical grade.

Handling and Purification of APG

APG exudates were collected from the stem of *Prunus armeniaca* (Malatya, Turkey), dried in oven at 60°C and powdered with a cutting mill (Pulverisette 19, Laval Lab Inc., Canada). Powdered gum was dissolved in hot water. Mucilageous solution thus obtained was filtered through a muslin cloth. APG was precipitated with acetone and then centrifuged at 3000 rpm. The precipitate was dried overnight at 60°C, milled and then sieved through 0.212 mm sieve. Fine powder of APG was kept in a desiccator for further experiments.

Preparation of tablets

The composition of the tablet formulations was shown in Table 1. Appropriate amounts of TNX and anhydrous lactose were mixed in a cubic blender (Aymes, Turkey) for 10 min and then was added the binder solution of APG purified as mentioned above. The mixture was extruded by passing through a 1.4mm sieve to form the TNX granules, dried in a ventilated air oven for 24 h at 50°C and then was sieved through 0.71 mm. After addition of magnesium stearate (1% w/w) the granules were mixed for 5 min then compressed into tablet form using a single punch tabletting machine (Yeniyurt, Turkey) equipped with different compression forces (1000, 1500, 2000 psi). For comparison, tablets containing GA and PVP as binding agents were prepared with the same procedure.

Table 1. Content of the formulations prepared by wet granulation method.

FORMULATION*	TNX (g)	Lactose (g)	GA (g)	PVP (g)	APG (g)
A_1	25	223.75	1.25	-	-
A_2	25	222.50	2.50	-	-
A_3	25	221.25	3.75	-	-
A_4	25	220.00	5.00	-	-
B_1	25	223.75	-	1.25	-
B_2	25	222.50	-	2.50	-
B_3	25	221.25	-	3.75	-
B_4	25	220.00	-	5.00	-
C_1	25	223.75	-	-	1.25
C_2	25	222.50	-	-	2.50
C_3	25	221.25	-	-	3.75
C_4	25	220.00	-	-	5.00

*Indicated for 250 g granule

Characterization of granules

TNX granules prepared by wet granulation method were investigated in respect to their flow properties.

Angle of repose and flowability

The angle of repose was calculated via fixed funnel method (Sinko, 1997). Calculations were made from the cone height (Eq. 1).

$$\text{Tangent}\,\alpha = \frac{h}{r} \qquad \text{(Eq. 1)}$$

α : angle of repose, *h:* height and *r* :radius (in centimetres).
Flowability of the granules was determined using an Erweka-GDT funnel type flow testing apparatus (Germany). 10g granules were run for each test.

Granular density and intergranular porosity
Granular density was measured in 6 replicates using a 25ml picnometer as reported earlier (Martin A, 1993). Xylol that neither penetrates into the internal pores nor dissolves the granules, was chosen as dispensing agent. The granular density and intergranular porosity (P%) were calculated (Gennaro, 1995; Lieberman, *et al*, 1989):

$$P\% = 1 - \frac{D_B}{D_G} \times 100 \qquad \text{(Eq. 2)}$$

Bulk density, tapped density and compressibility (Carr's index)
TNX granules (10g) were placed into Stampfvolumeter („J.Engelsman AG Apparatebau, Germany) and the volume was recorded (V_B). After 100 times of tapping volume was recorded (V_T) again. The bulk (D_B) and tapped densities (D_T) as well Carr's index (CI) were calculated with the Eqs. 3-5 (Gennaro, 1995; Lieberman, *et al*, 1989);

$$D_B\,(g/cm^3) = \frac{\text{Weight of granule}}{V_B} \qquad \text{(Eq. 3)}$$

$$D_T\,(g/cm^3) = \frac{\text{Weight of granule}}{V_T} \qquad \text{(Eq. 4)}$$

$$CI\,(\%) = \frac{D_T - D_B}{D_T} \times 100 \qquad \text{(Eq. 5)}$$

Characterization of tablets

Weight variation
The weight variation indicating the tablet uniformity was determined according to United States Pharmacopoeiae (USP XXIV), with 10 replicates for each series (USP 24, 2000).

Friability
The friability studies were conducted with a Roche friabilator (Aymes, Turkey). Twenty tablets were weighed (W_1) and placed into the friabilator (25 rpm, 100 revolutions) (USP 24, 2000). The tablets were reweighed (W_2) and friability of TNX tablets (F%) was calculated with the Eq. 6;

$$F\% = \frac{W_1 - W_2}{W_1} \times 100 \qquad \text{(Eq. 6)}$$

Crushing strength
Crushing strength of tablets was determined using Vankel VK-200 crushing strength tester (Varian Inc., USA) (Gennaro, 1995; Lieberman, *et al*, 1989). Ten tablets from each formulation were used and the mean values were expressed in Newton (N).

Disintegration time
Disintegration time of TNX tablets were individually measured in distilled water maintained at 37±0.5°C using a disintegration tester apparatus (Aymes, Turkey) (USP 24, 2000). Disintegration time was completed when no residue of the unit remained on the screen of the test apparatus.

Six measurements were run for each tablet formulations. The mean disintegration time and standard deviation were calculated.

In vitro drug release
The dissolution rate of TNX from tablets was determined using the paddle method (British Pharmacopoeia, 2001). Phosphate buffer (pH 6.8, 37±0.5°C, 50 rpm) was used as dissolution medium. An aliquot of sample withdrawn at specified intervals was filtered through a 0.45μm nylon disc filter and analyzed spectrophotometrically at 368 nm for TNX content.

Statistical analysis
Statistical analyses were made by the Student's *t* test and $P<0.05$ was considered to be indicative of significance.

Results and Discussion

The angle of repose of a powder provides an insight to the magnitude of the cohesiveness. The angle of repose and flow time together with percent compressibility constitute important parameters for determining the flow behaviour. Since TNX is known to possess poor flowing and compressing properties, prior to tabletting process TNX granules were examined in this respect. Angle of repose values of all the granule formulations were found $\leq 30°$, indicating that an improvement was achieved in the flowability characteristics of TNX (Lieberman, *et al*, 1989; Martin, 1993) which were supported by flow time results (1.0-1.2 secs) ($p>0.05$). The granule formulations containing TNX had an excellent flow and compressibility as indicated by low value of Carr's index ($\leq 30\%$) (Table 2).

Intergranular porosity of the measured granules measured varied from 54.73% to 61.44% showing appropriate values for true density (Table 2) as well.

Table 2. Flowability and porosity results of granules

FT: flow time; *AP*: angle of repose; D_B: bulk density; D_T: tapped density; *CI*: Carr's index; D_G: granule density; *P*: intergranular porosity

FORMULATION	*FT* (sec)	*AP* (°)	D_G	D_T	D_B	*CI* (%)	*P* (%)
A_1	1.1±0.1	25.4±0.9	1.45±0.01	0.73±0.00	0.64±0.00	12.72	56.11
A_2	1.1±0.1	25.3±0.7	1.47±0.01	0.71±0.01	0.62±0.00	12.04	57.79
A_3	1.0±0.0	25.3±0.8	1.47±0.01	0.72±0.00	0.64±0.00	11.63	56.33
A_4	1.0±0.0	25.4±0.8	1.47±0.01	0.72±0.00	0.63±0.00	12.29	56.88
B_1	1.0±0.1	25.8±0.9	1.45±0.01	0.74±0.00	0.66±0.01	11.48	54.73
B_2	1.0±0.0	25.6±0.8	1.47±0.01	0.73±0.01	0.65±0.00	11.33	55.68
B_3	1.0±0.1	25.1±0.2	1.45±0.02	0.74±0.01	0.65±0.00	11.58	55.23
B_4	1.0±0.1	25.5±0.8	1.44±0.01	0.74±0.01	0.65±0.00	11.25	54.78
C_1	1.2±0.0	25.5±0.9	1.45±0.01	0.63±0.00	0.56±0.00	12.63	61.44
C_2	1.1±0.1	25.3±0.6	1.45±0.01	0.75±0.00	0.66±0.00	12.42	54.73
C_3	1.0±0.0	25.8±0.9	1.45±0.01	0.68±0.00	0.59±0.01	12.71	59.13
C_4	1.0±0.1	25.9±0.8	1.44±0.01	0.73±0.00	0.63±0.00	13.33	56.33

All of the results attained from tablets were in accordance with the data given by USP. The weight of tablets weigh was ranged from 199.2 to 199.8mg. The relative standard deviation of the formulations was found to be within the pharmacopoeial limits (USP 24, 2000).

The friability is known as the highest limit of acceptability for pharmaceutical products is 1% (Rudnic, and Kottke, 1996). The friability values were found to be < 1% with the exception of those which were applied 2000psi (A_1-A_3, C_1-C_3 and B_1) (Fig. 1). In each case, the friability decreased as the binder concentration increased. This collaborates the findings reported in the literature (Kolter, and Flick, 2000).Tablet formulations with 2000psi containing GA and APG were considered out of scope due to their high friability values (Fig 1). The friability results attained from A_1-A_4 and C_1-C_4 formulations are 26.94%, 25.97%, 5.75%, 0.76%, 27.89%, 26.08%, 6.57% and 0.90%, respectively.

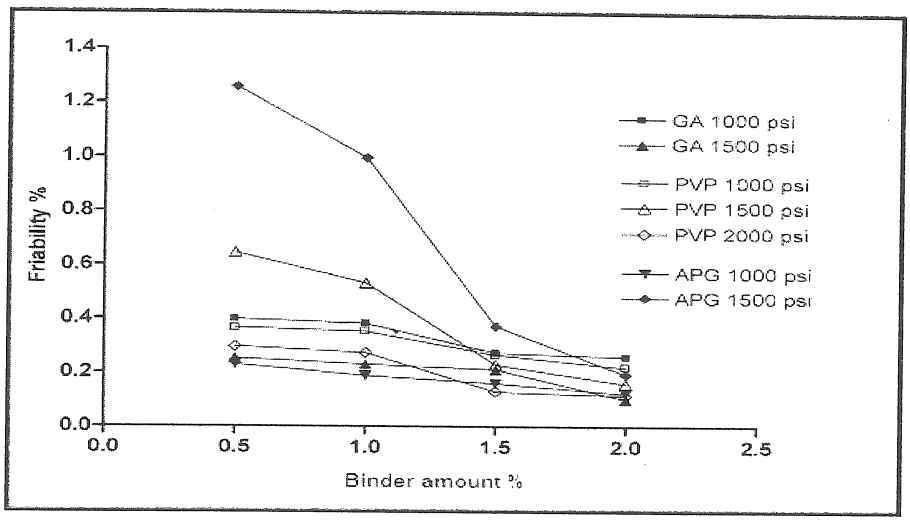

Figure 1. The effect of binder amount on friability of tablets

The crushing strength of tablets are shown in Fig 2. Depending on the increase in binder concentration, friability was decreased, moreover crushing strength and disintegration times were increased (Table 3). It was reported that friability is opposed to crushing strength and disintegration time (Nada, and Graf, 1996). The tablets which were 1500psi applied gave the highest crushing strength and disintegration time. It was reported that disintegration time and crushing strength were increased with the increase in pressure applied (Velasco, *et al.*, 1999). But in the case of tablets prepared under 2000 psi, crushing strength and disintegration time were decreased due to the high friability. This was attributed to the natural gums such as APG and GA, exposed to plastic deformation due to the high pressure applied during wet granulation process that causes decrease in tablet resistance (Smith, 1959).

Table 3. Mean disintegration time (sec) of formulations

Compaction pressure (psi) / Formulations	1000	1500	2000
A_1	256±3	262±8	214±7
A_2	258±2	268±5	228±4
A_3	260±8	272±8	235±6
A_4	276±5	308±6	248±8
B_1	277±5	280±8	260±5
B_2	292±6	294±8	283±4
B_3	300±8	302±10	290±2
B_4	303±4	310±7	298±4
C_1	312±8	315±6	210±5
C_2	321±4	322±6	218±8
C_3	368±6	370±8	238±9
C_4	417±11	420±8	245±7

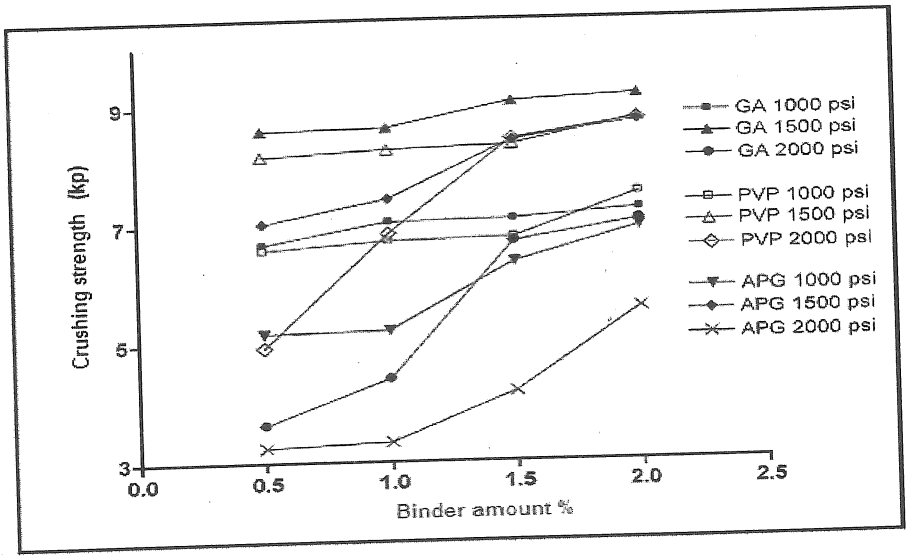

Figure 2. The effect of binder amount on crushing strength of tablet

According to *in vitro* release results, maximum TNX release was obtained with the tablets containing PVP as binder. Tablet formulations prepared using APG as a binder, showed faster TNX release than those containing GA ($p<0.05$). TNX release was reduced in all tablet formulations with the increase the binder concentration and pressure applied ($p<0.05$) (Fig. 3-5).

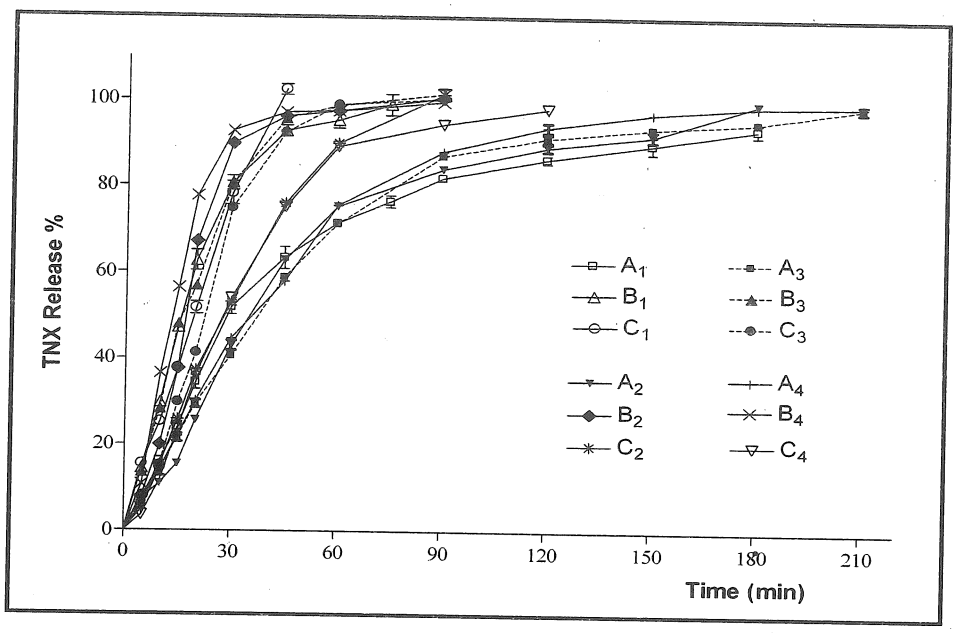

Figure 3. *In vitro* release profiles of the tablets prepared by wet granulation using 1000 psi pressure

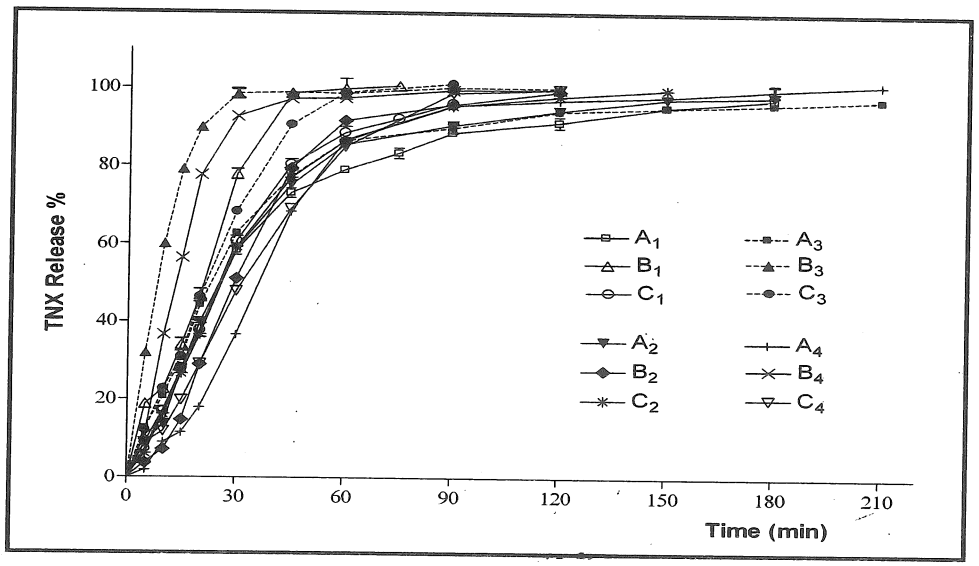

Figure 4. *In vitro* release profiles of the tablets prepared by wet granulation using 1500 psi pressure

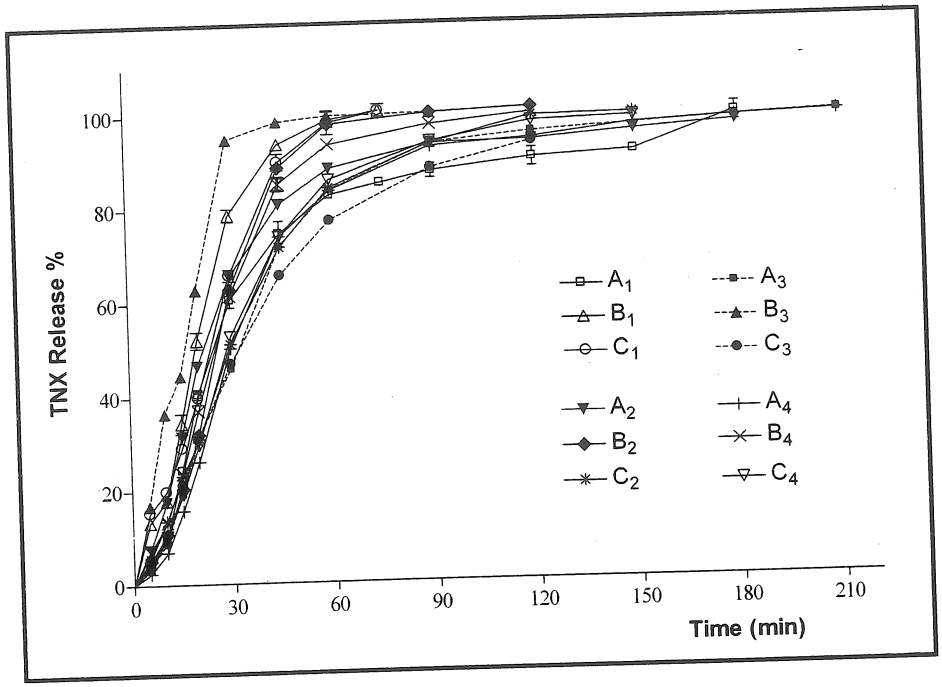

Figure 5. *In vitro* release profiles of the tablets prepared by wet granulation using 2000 psi pressure

As a conclusion, APG was found to be a suitable binder in the concentrations of 0.5-2% however high compression forces should be avoided during preparation of tablets.

Özet: Bu çalışmada, *Prunus armeniaca* (kayısı) dan elde edilen kayısı zamkının bağlayıcı özelliği, yaş granülasyon metodu kullanılarak hazırlanan tabletlerde araştırıldı. Çalışmamızda model ilaç olarak tenoksikam seçildi. Kayısı zamkının bağlayıcı özelliği arap zamkı ve polivinil pirolidon ile karşılaştırıldı. Ayrıca farklı basım kuvvetinin tablet özelliklerine etkisi de araştırıldı. Sonuç olarak kayısı zamkı % 0.5-2 konsantrasyonunda bağlayıcı olarak kullanılabileceği ancak tabletlerin basılmasında yüksek basım kuvvetinden kaçınılması gerektiği saptandı.

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