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## Influence of Granule Size and Lubricant Concentration on the Dissolution of Paracetamol Tablets

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**The effects of granule size and concentration of magnesium stearate as lubricant on the dissolution rate of paracetamol tablets were studied. The results obtained show that dissolution rate was increased as the granule size of the tablet was increased for tablets prepared with 1.5% magnesium stearate as lubricant. However, tablets prepared with different granule size, exhibited no pronounced effect on the dissolution characteristics when concentration of magnesium stearate was used as 0.75%.**

The relationship between granule size and dissolution rate for a number of drugs was previously reported<sup>1-4</sup>. In another study, Finholt and Solvang<sup>5</sup> have pointed out that the dissolution rate of phenacetin tablets was increased as the particle size was decreased. Dissolution may be affected by incorporation of a lubricant<sup>6</sup>. Hydrophobic lubricant decreases the effective drug-solvent interfacial area, which results in reducing wettability and thereby prolonging its dissolution<sup>7</sup>. Hasan *et al.*<sup>10</sup> indicated that the dissolution time of paracetamol tablets was increased with the decrease of the granule size in presence of magnesium stearate. The present authors in their earlier study found that dissolution rate of paracetamol tablets containing 1.5% magnesium stearate increased as the granule size increased<sup>8</sup>. The report assumed that layer of granules undergo a breakdown during compression, yielding a larger surface area some of which are not covered by the insoluble lubricant (magne-

sium stearate). The present study concerns with the dissolution characteristics of compressed paracetamol tablets, prepared with three different granules and in presence of varying concentrations of a hydrophobic lubricant, magnesium stearate.

Paracetamol IP was obtained as a gift sample from Duphar-Interfran Ltd, Mumbai. Excipients used in preparing the tablets were starch, talc, polyvinylpyrrolidone (PVP), alcohol and magnesium stearate and all were of IP grade. Weighed quantities of paracetamol, starch, and talc were mixed for 30 min and kneaded with 40% w/v solution of PVP in alcohol. The mixture was granulated by passing through sieve no. 16 followed by drying at 50-55° for 10-12 h. The dried granules were separated by sieves 16, 22 and 30 into three parts. The sized granules of each lot was subdivided into two portions and mixed with 1.5% and 0.75% magnesium stearate, respectively. The tablets were compressed on a single punch tablet machine at a constant compression force with calculated average weight of a tablet equiva-

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TABLE 1: EFFECT OF GRANULE SIZE ON DISSOLUTION OF PARACETAMOL TABLETS.

Time (min)	Cumulative percentage dissolved					
	Using 1.5% magnesium stearate			Using 0.75% magnesium stearate		
	Granule size (Sieve 30)	Granule size (Sieve 22)	Granule size (Sieve 16)	Granule size (Sieve 30)	Granule size (Sieve 22)	Granule size (Sieve 16)
5	4.91±0.28	5.74±0.38	9.71±0.92	7.09±0.22	7.48±0.78	8.50±1.10
10	11.2±0.44	13.7±0.99	27.6±1.19	26.1±0.21	24.9±0.86	30.4±0.74
20	23.0±0.42	27.8±0.72	39.4±1.34	38.2±1.03	38.4±1.24	41.8±0.89
30	33.5±0.98	47.7±1.64	55.4±0.80	53.4±1.51	58.2±1.15	57.0±0.76
45	58.0±1.15	78.1±1.09	85.0±1.32	82.9±1.31	85.0±1.07	86.2±1.09
60	64.4±1.12	85.2±1.33	94.3±0.98	91.3±1.27	93.3±0.76	95.1±1.17
75	72.8±1.22	95.4±1.51	96.8±0.72	96.0±1.31	96.0±0.58	97.1±0.43
90	77.2±1.01	96.5±0.28	96.0±0.38	96.5±1.41	97.1±0.52	96.8±0.49

Note-Each value represents mean±SD (n=3). The tablets were prepared with 1.50 and 0.75% of a lubricant, magnesium stearate.

lent to 500 mg of paracetamol.

For the dissolution time determination, the method of Rotating Basket Apparatus (USP 21)<sup>9</sup> was employed. Simulated gastric fluid, pH=1.2 at 37±0.5° was used. Samples of 1 ml quantities were withdrawn at 5, 10, 20, 30, 45, 60 and 90 min intervals and were diluted with 10.6 ml NaOH (0.1N) and water and analyzed spectrophotometrically at  $\lambda_{max}$  257 nm. The content of paracetamol was calculated taking 715 as the value of A (1%, 1cm) at 257 nm. Statistical analysis was performed with Excel 2002 (Microsoft Office XP). Two-factor without replication ANOVAs were performed on percentages dissolved at time intervals. The within groups effect was time intervals and between group effect was granule sizes at a particular time.

The results are given in Table 1. The results of dissolution in terms of cumulative percentage release of paracetamol at the definite intervals for three series of tablets prepared with two different concentrations of magnesium stearate, namely 1.5% and 0.75%, respectively are shown in the Table 1.

As shown in Table 1, with 1.5% magnesium stearate, dissolution time was increased with decrease of the granule size (higher sieve number). Dissolution times for 50% release ( $t_{50}$ ) were 26.5, 31 and 40.5 min for granules prepared using sieve numbers 16, 22 and 30, respectively. All the values of the mean percentage release at various time inter-

vals up to 1 h between three types of granules differed significantly at P=0.039 (DF=2, F ratio=4.52). Although these results were not in agreement with others previously reported<sup>2,5</sup> but in agreement with the findings of recent authors<sup>8,10</sup>. This confirms that the assumptions of the authors<sup>8,10</sup> that larger granules yield a larger surface after breakdown, some of which are not covered by hydrophobic lubricant.

Table 1 further shows the dissolution obtained with tablets in presence of 0.75% of the lubricant, magnesium stearate were not significantly different between tablets of different granule sizes. Dissolution times for 50% release ( $t_{50}$ ) were 25.5 min for tablets prepared with granule sizes 16 and 22, and it was 26.5 min for granule size 30. Neither values of percentage release with different granule sizes were significant at P=0.26 (DF=2, F ratio=0.24). It is therefore concluded that during paracetamol tablet formulation factors such as granule size and concentration of hydrophobic lubricant influence the dissolution characteristics of the tablet dosage form. The dissolution rate is not directly proportional to the decrease in size of the granules but to the effective dissolution medium interfacial area and also indirectly to the concentration of hydrophobic lubricant.

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## Wound Healing Activity of *Chandanadi Yamak* in Rats

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*Panchagavya* is a term used in Ayurveda to describe the five important bovine products, milk, curd, ghee, urine and dung. Several formulations based on *panchagavya* are reported in Ayurvedic texts. One such formulation, *Chandanadi Yamak* was tested in the present study for its topical wound healing activity. Studies were conducted in male Wistar rats. Two wound models, incision wounds for tensile strength and excision wounds for wound contraction were employed along with histopathological evaluation. The application of the test formulation alone promoted wound contraction and reduced the time for wound closure showing healing potential comparable to marketed framycetin sulphate cream (1% w/w). The histological studies reveal complete healing with the test formulation showing good keratinization, epithelialization, fibrosis and angiogenesis. The present study demonstrates the wound healing potential of the test formulation.

Wounds are visible results of individual cell death or damage, and can be classified by site, size, depth, cause (surgery/accident) or circulatory failure<sup>1</sup>. Wound healing is a process, which is fundamentally a connective tissue response. Initial stage of this process involves an acute inflammatory phase followed by synthesis of collagen and other extracellular macromolecules, which are later remodeled to, from a scar<sup>2</sup>. Several factors delay or reduce wound healing, including bacterial infections, necrotic tissue, interference with blood supply, lymphatic blockage and diabetes mellitus. Generally if the above conditions could be altered

by any agent, an increased healing rate could be achieved<sup>3</sup>.

*Chandanadi Yamak* is a *panchagavya*-based polyherbal formulation, claimed to promote wound healing in traditional practices. *Panchagavya* is a term used to refer the five important bovine products, milk, curd, ghee, urine and dung. Several formulations based on *panchagavya* are reported in Ayurvedic texts and few reports concerning the evaluation of their pharmacological activities are reported in literature<sup>4-6</sup>. The present communication deals with the evaluation of wound healing activity of *Chandanadi Yamak* in terms of wound contracting ability, wound closure time, regeneration of tissues at wound site, tensile strength of wound and histopathological characteristics. The ingredients of

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