indicate high accuracy and precision of the method. In HPLC the calibration curve is linear in the range 4 - 40µg/ml, with correlation coefficient R = 0.9996. The reproducibility of the method was checked by inter and intra assay variations and the accuracy of the method was checked by % deviation from actual concentration, both were found to be less than 5%. The content of the compound was calculated from the average peak height of six replicates by using the formula

Unknown conc. = KxPeak height + B,

Where K = 2.7276 and B = 0.7111 (for tlc-densitometry)

and K = 6.6940 and B = -0.3305 (for hplc method)

The present methods provided sensitive assay methods with proper resolution of 82/205. No interference from the other constituents of formulations were observed. Table I shows the inter and intra assay variations results.

ACKNOWLEDGEMENTS

The authors thank Mrs. M. Chaudhry for her technical assistance.

REFERENCES

1. Mathur, K. B., Sharma, S. D., Haq, W., Kundo, B., Raghubir, R., Patnaik G. K. and Dhawan, B. N., Indian Patent No. 173568 dt. 19.10.89.
2. Mathur, K. B.; Dhotre, B. J.; Raghubir, R.; Patnaik, G. K.; and Dhawan, B. N. **Life Sciences**, 1979, 25, 2023.
3. Raghubir, R,; Patnaik, G. K.; Dhotre, B. J.; Mathur, K. B.; Dhar, M. M.; and Dhawan B. N. **Ind. J. Pharmacol.** 1979, 11, 42.
4. Raghubir, R.; Patnaik, G. K.; Sharma, S. D.; Mathur, K. B.; and Dhawan, B. N. In : Dhawan, B. N. ed. Current Statud of Centrally Acting Peptides, Oxford : Pergamon Press. 1982, 61.
5. Mathur, S. K. and sinha N., XV Annual Conference of Society of Toxicology, Calcutta, November, 1996, 15.

Performance evaluation of Tamarind seed polyose as a binder and in sustained release formulations of low drug loading

D. KULKARNI, A. K. DWIVEDI AND S. SINGH

Divn. of Pharmaceutics, Central Drug Research Institute, Lucknow - 226001

Accepted 14 November 1997

Received 6 May 1997

Evaluation of tamarind seed polyose as a binder for tablet dosage forms was taken up for the wet granulation as well as direct compression methods. The drug release sustaining properties of tamarind seed polyose polymer were also studied using 5 mg of terbutaline sulphate matrices. The results indicated that tamarind seed polyose could be used as binder for wet granulation and direct compression tableting methods as well as a suitable polymer for sustained release formulations of low drug loading.

THE extraction process for Tamarind Seed Polyose (TSP), a natural polymer[1,2] obtained from the seeds of *Tamarindus Indica* has been developed at this Institute. An assessment of its bindings properties in wet granulation method and as a dry binder in tablet dosage forms was undertaken vis-a-vis the binding properties of binders such as starch, gelatin, methyl cellulose, sodium carboxymethyl cellulose and polyvinyl pyrrolidone. Tablets prepared were evaluated for uniformity of weight. hardness, friability[3], and disintegration tests[4]. A recent study showed slow drug release for tablets compressed form TSP with high drug loading of verapamil hydrochloride[5,6]. The present study also reports the use of TSP as a polysaccharide polymer in the design of solid controlled release dosage

*For correspondence

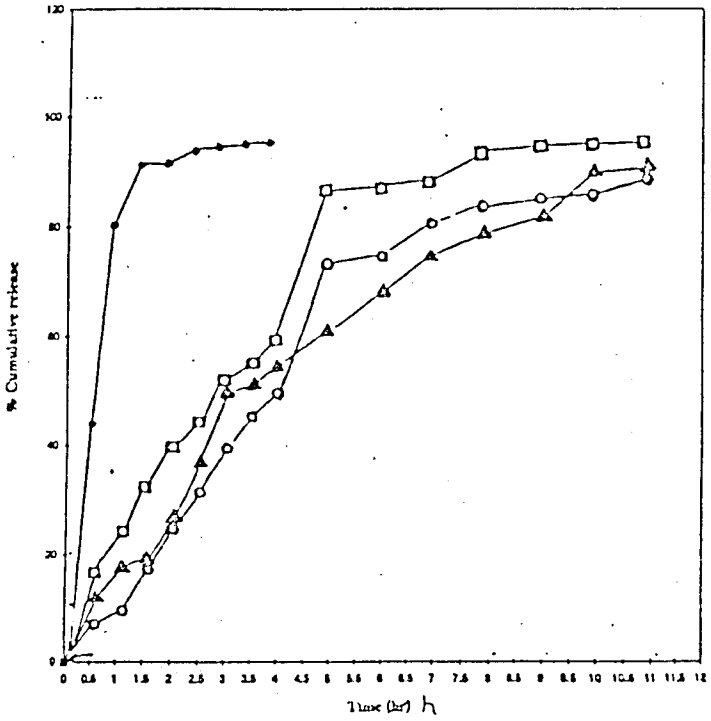

Fig 1 A : *In vitro* release profiles of matrices of terbutaline prepared by direct compression using TSP o---o---o D.P. (1:9), Δ---Δ---Δ D : P (1:24), and marketed products ●---●---● M(C), □---□---□ MSRT

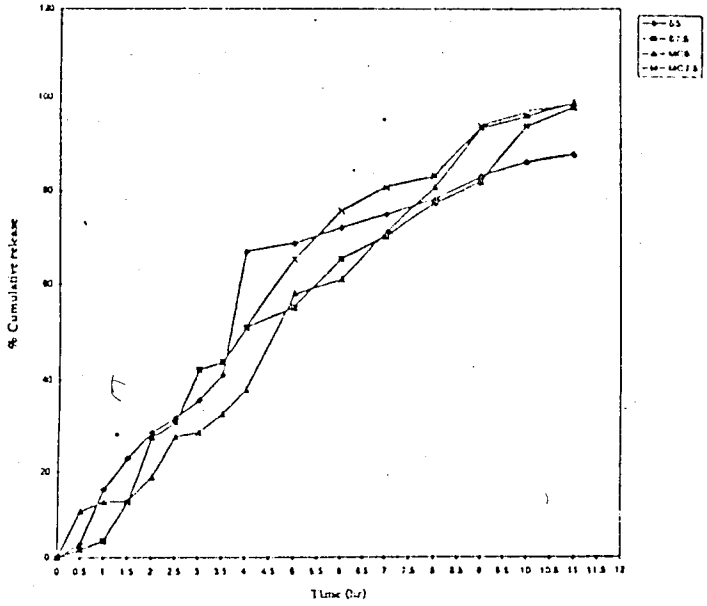

Fig 1 B : *In vitro* percent cumulative release data of formulated terbutaline sulphate matrices by the wet granulation method using tamarind seed polyose as polymer and starch (5 & 7.5% w/v) and methyl cellulose (5 & 7.5% w/v) as binders

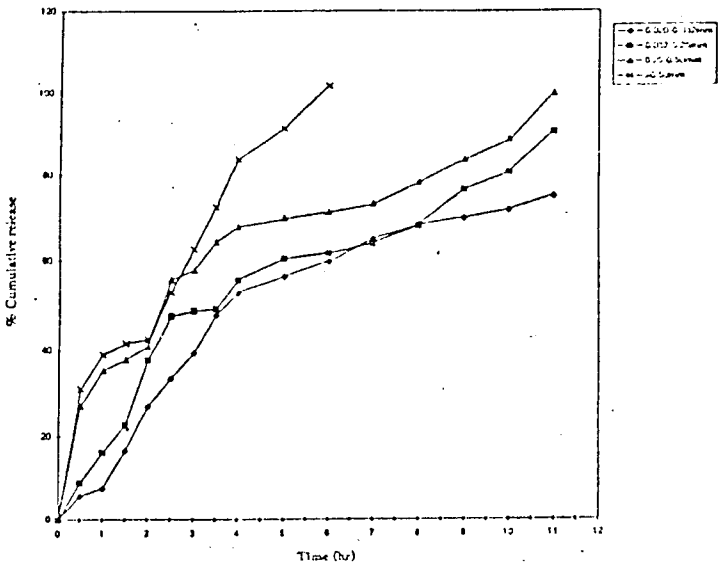

Fig 1 C : *In vitro* percent cumulative release data of formulated matrices terbutaline sulphate by direct compression method using tamarind seed polyose of different particle size fractions in drug to polymer ratio 1:19

forms with low drug loading. Terbutaline sulphate[7] was chosen as model drug. The effect of different parameters on drug release was investigated. Comparison was made hydroxy ethyl cellulose (HEC), the commercially available polysaccharide polymer and the marketed conventional and sustained release preparations of terbutaline sulphate (TS).

Terbutaline sulphate was a generous gift of Astra-IDL Bangalore (India). The polymer used hydroxethyl cellulose was obtained from Fluka AG, Switzerland. Tamarind seed polyose was prepared on laboratory scale[1] at CDRI. The other polymers and lactose and magnesium stearate used were of pharmacopoeal grade. All other reagents and solvents were of analytical grade (E. Merck India Ltd.). Terbutaline sulphate sustained release tablet [SRTM] [5 mg] [Bricanyl Durules] and the conventional tablet Bricanyl [2.5 mg] were purchased from the market. All tablets were prepared on the single punch Korsch tabletting machine. The hardness of all the tablets was measured using a Mcnsanto Hardness Tester.

Tablets (350 mg) of lactose powder were prepared by using 10 % aq. solution of each binder in wet granulation process or by taking 2.5, 5.0, 7.5, 10.0, 12.5 % by weight

concentration of each binder polymers in dry granulation method. 1% magnesium stearate was used as lubricating agent.

To study the sustaining effect of TSP, matrices were prepared by compressing physical blends of the drug [TS] (5 mg) and the polymer in the appropriate drug g to polymer ratio using magnesium stearate as lubricant and keeping the angle of repose 35 ± 5°. Similarly tablets of TS (5mg) were also prepared by wet granulation method using 5 % or 7.5 % w/v starch or methyl cellulose as granulating agent.

Dissolution studies of the formulated/ commercially available sustained release tablets were carried out using the Sartorius Dissolution Simulator (Type SM 16751 Fab. NR. 2339, Sartorius-GMBH, Gottingen, Federal Republic of Germany) maintained at 37°. The study on each formulation was carried out for 4 h at pH 1.2 followed by replacement of the buffer by pH 7.4 buffer for 7 h. The terbutaline concentrations were assayed at 276 nm using the Shimadzu UV-Vis 260 spectrophotometer (Japan). The effect of particle size on *in vitro* release of the drug was determined using the method described above except the study on each formulation was carried out by a gradual change in pH from 1.2 to 8 over a period of 8 h at fixed time intervals by gradual addition of disodium hydrogen ortho phosphate.

The properties of TSP as a binder in tablets have been investigated as early as 1958 by Patel *et al.*[8]. However, at CDRI. a new process has been developed to yield the polymer of pharmaceutical grade. The utility of this polymer as a binder in tablet dosage forms was studied.

All tablets confirmed to the test for uniformity of weight. For tablets prepared by wet granulation with 10 % binder solution, the hardness [kg/sq.cm] of tablets using methyl cellulose was the least [5.6 ± 0.8] followed by starch [7.5 ± 0.9] TSP [8.2±1.1] polyvinyl pyrrolidone [8.88±0.8] and sodium carboxymethyl cellulose [9.44±0.67]. The percent friability was found to be maximum for NaCMC [0.82]. While with the other binders it was almost the same [about 0.45]. TSP binder at 10% concentration showed disintegration time of tablets to be the same as MC, NaCMC and PVP [about 25 min.].

In all the binders studied the hardness of tablets was found more or less same [3.5 - 5 Kg/sq. cm] except for PVP. The binders MC [3-7 min.], starch [0.8-3.3 min.] showed disintegration time of tablets similar to that of TSP [1.2-4 min.] tablets. Tablets prepared using NaCMC showed on an average higher friability values than other binders, followed by starch, TSP and PVP.

Tablets of terbutaline sulphate were prepared by using different amounts of polymer HEC for optimization of drug : polymer ratio. From *in vitro* studies it was found that from drug to polymer ratio 1:19 the drug release was sustained for 11 h. The matrices prepared by 1:19 and 1:24 gave a constant release of the drug throughout the study period and no significant difference was found between the two formulations. These two ratios of drug to polymer (1:19 and 1:24) were also extended to the polymer TSP. *In vitro* release studies indicated that TSP could also sustain the release of drug from matrices, with low drug loading, over the study period [Fig. 1A] and it was more continuous or gradual as compared to the matrices of HEC or the marketed sustained release product [MSRT].

Two commonly used binders, starch and methyl cellulose, were chosen as granulating agents in the concentrations of 5.0 and 7.5 % w/v, *In vitro* release profiles are shown in the figures 1B. A comparison of the *in vitro* release profiles of matrices prepared using direct compression and wet granulation techniques for the polymer TSP showed no influence of formulation techniques. *In vitro* release profiles of matrices prepared using these aforementioned particle size ranges [0.5-25, 0.25-0.032 and 0.032-0.020 mm.] for the polymer TSP [Fig. 1C] exhibited a good correlation for *in vitro* release profiles, i.e. a decrease in particle size was found to decrease the release rate of the drug.

All matrices were found to release the drug following the Higuchi equation[9], i.e. the percent cumulative release was directly proportional to the square root of time.

A comparison of parameters studied indicated that TSP can be used as a binder for wet granulation and direct compression tableting methods. In *in vitro* observations, TSP proved to be a suitable polymer for sustained release formulations of low drug loading. The formulations exhibited a better and more consistent release as compared to the reference formulation MSRT.

ACKNOWLEDGEMENT

The authors are grateful to CSR, New Delhi, for Senior Research Fellowship to one of them (D. K.), to M/s Astra IDL for supply of Terbutaline sulphate and to Mrs. M. Chaudhary for her technical assistance.

REFERENCES

1. Nandi, R. C., Sarin, J. P. S. and Khanna, N. M., A Process for the Preparation of Polyose from the Seeds of Tamarindus indica, Ind. Pat. No. 142092, 1975.
2. Khanna M, Nandi R. C. and Sarin J. P. S., **Indian Drugs**, 1987, 24, 268.
3. Marshall, K., In; Theory and Practice of Industrial Pharmacy, 3rd Ed, Verghese Publishing House, Bombay, 1987, 88.
4. Pharmacopoeia of India, 3rd Ed, Controller of Publications, New Delhi, vol. II, 1985, A-121.
5. Dwivedi A. K., Kulkarni D. and Singh S., A Process for the Preparation of Sustained Released Tablet Formulation of Verapamil Hydrochloride Using Polysaccharide Polymers. Indian Patent Application No. 433/DEL/95 Dated 14.3.95.
6. Kulkarni D., Dwivedi A. K., Sarin J. P. S. and Singh S., **Ind. J. Pharm. Sci.**, 1997, 59, 1.
7. Martindale : The Extra Pharmacopoeia, 30th Ed., The Pharmaceutical Press, London, 1993, 1257.
8. Patel R. P. and Joshi G. J., **Indian J. Pharma.**, 1958, 20, 279.
9. Higuchi T., **J. Pharm. Sci.**, 1963, 52, 1145.

Spectrophotometric Determination of Atenolol and Timolol Dosage forms *via* Charge-transfer complexation

S. P. AGARWAL*, VASUDHA SINGHAL AND ANITA PRAKASH
Dept. of Pharmaceutics, Faculty of Pharmacy,
Jamia Hamdard (Hamdard University), New Delhi - 110062

Accepted 4 September 1997
Received 13 May 1997

A spectrophotometric method is described for the determination of atenolol and timolol as bulk drug and in dosage forms by complexation of the drug with choranilic acid. Job's method revealed a 1:1 complexation between the drug and choranilic acid. Quantitative recoveries were obtained from commercially available dosage forms.

TIMOLOL maleate is a β-blocker used in the treatment of hypertension, glaucoma and for prophylaxis after myocardial infraction[1]. Atenolol is popular in the therapy of essential hypertension. For atenolol and timolol maleate, USP[2] and IP[3] describe a nonaqueous titration method using 0.1 N perchloric acid whereas the assay procedure for atenolol tablets and timolol opthalmic solution is based upon the extraction of the drug and determination of its absorbance[2,3]. For timolol maleate tablets either alone or in combination with hydrochorthiazide an HPLC assay procedure is given[2]. A reversed phase HPLC method for the simultaneous determination of atenolol and nifedipine in tablets[4] and a spectrophotometric method for timolol maleate in eye drops[5] have been described.

Charge-transfer complexation has been found to be a useful technique for the determination of many drugs which contain electron donor groups. The use of chloranilic acid has been described in the determination of several alkaloids[6,7] in dosage forms. Here we wish to describe a simple and sensitive spectrophotometric method for the

*For correspondence