Effect of Dispersant on the Dissolution of Chloramphenicol from a Capsule Formulations

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The effect of Sodium Starch Glycolate (SSG), a dispersant on the dissolution of chloramphenicol from capsules was studied. Chloramphenicol was formulated into capsules with SSG and the capsules were evaluated for drug content, disintegration time and dissolution rate. Marked increase in the dissolution of chloramphenicol was observed when SSG was included in the capsule formulation. This formulation gave fast and rapid dissolution of chloramphenicol fulfilling the USP 23 and B.P. 1993 dissolution requirement.

THE poor dissolution characteristics of relatively insoluble drugs has long been a problem to the pharmaceutical industry. Several reports have been reported to enhance the dissolution and bioavailability of poorly soluble drugs[2,5]. Chloramphenicol an important antimicrobial drug, is sparingly soluble in water and aqueous fluids and its oral absorption is dissolution rate limited. USP 23[6] and B.P. 1993[1] have prescribed a dissolution rate specification for chloramphenicol capsules. Sodium starch glycolate, a dispersant has been used earlier to increase the dissolution rate of piroxicam from capsule formulations[3]. In the present investigation, the effect of Sodium starch glycolate, a dispersant on the dissolution of chloramphenicol from capsule formulation was studied. The dissolution test of chloramphenicol from capsule formulation was studied. The dissolution test of chloramphenicol capsules is not included in I.P[4] at present, but included in B.P. and U.S.P.

Sodium starch glycolate, the sodium salt of a carboxymethyl ether of starch, is official in USP 23-NF 18, B.P. 1993 and I.P. 1985, Addendum (II), 1991. In the present work, sodium starch glycolate I.P was used. It is obtained from local market (It's 2% dispersion in cold water settles, on standing, to give a highly hydrated layer). Lactose I.P was used as a diluent. Magnesium stearate I.P and Colloidal silicon dioxide I.P were used as lubricants. Hard gelatin capsule shells I.P and Chloramphenicol B.P were used.

The composition of various batches of powder mix for encapsulation is given in **Table I**. In each case the required amount of drug, which was passed through sieve no 40 and other additives (previously dried), which were passed through sieve no 80 were mixed thoroughly by geometric dilution technique. The powder mixture was then filled into gelatin capsules (size 1) using Scorpio semi automatic capsule filling machine. The batch size of capsules was 10,000 and temperature and relative humidity of the filling room were 25°C and below 40%, respectively. The capsules were evaluated for drug content, disintegration and dissolution rate.

Chloramphenicol content of the capsule was determined by spectrophotometrically as specified in B.P. Disintegration times were determined using Virgo tablet disintegration test machine USP standard using distilled water as the fluid.

Dissolution of chloramphenicol from various capsules was studied in a programmable tablet dissolution tester of Electrolab, Model TDT-06P(USP XXII) apparatus as per the USP 23 dissolution rate test

Table 1 : Formulation of chloramphenicol capsules (size 1)

Ingredients	weight (mg) / capsules			
	CAP1	CAP2	CAP3	CAP4
Chloramphenicol	250	250	250	250
Lactose	—	134.5	109.5	84.5
S.S.G.	—	—	25	50
magnesium Stearate	4	4	4	4
Colloidal silicon dioxide	1.5	1.5	1.5	1.5

Table 2 : Time and percentage of dissolution rate

batch code	Drug content (mg)	50 T (minutes)	30 (minutes) (%dissolved) (as per USP)	45 (minutes) (%dissolved) (as per B.P)
CAP1	242	14.30	58.30	58.80
CAP2	248	12.05	69.40	69.00
CAP3	240	9.30	86.50	86.40
CAP4	246	7.75	99.40	99.40

* Mean of 3 trials (18 capsules).

* T^{50} : Time taken for 50% dissolution (minutes).

(apparatus 1) prescribed for chloramphenicol capsules. In each test 900 ml of 0.1N hydrochloric acid, one capsule, a speed of 100 rpm and a temperature of 37°+/- 0.3°C were employed. A 5 ml aliquot of dissolution medium was withdrawn at different time intervals. Suitably diluted and assayed for chloramphenicol content by measuring extintion at about 278 nm. the results are given in **Table 2.**

All capsules prepared were found with in the compendial limits in respect to chloramphenicol content and disintegration of capsules. Capsules of batches CAP1 and CAP2 prepared with and without Lactose did not comply the dissolution test as per B.P. and U.S.P. Capsules of batches CAP3 and CAP4 prepared with lactose as diluent and sodium starch glycolate as dispersant showed much higher dissolution rate. The capsules ofbatch CAP4 showed 90% dissolution level in 10 minutes. The rate of dissolution was found to be directly proportional to the SSG content in the formulation. The rapid dispersal of the capsule contents might have resulted in rapid dissolution of the drug. Capsule formulations CAP3 and CAP4 (prepared) fulfilled the USP 23 and B.P 1993 dissolution requirement. For drugs like chloramphenicol, which is usually administered for a short duration in acute cases, the extent and rate of dissolution are crucial absorption parameters. The enhanced dissolution of chloramphenicol could be achieved from rapidly dissolving batch(s) capsules CAP3 and CAP4.

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