DETERMINATION OF THE ANHYDROUS MORPHINE CONTENT OF AROMATIC CHALK WITH OPIUM MIXTURE BP

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The British Pharmacopoeia (1980a) monograph for aromatic chalk with opium mixture contains no assay for anhydrous morphine. A suitable method is now described: A 5.0 ml portion from the homogeneous preparation was mixed with 3 ml 3M HCl and 5 ml water and allowed to stand for 5 mins until the effervescence had subsided. 15 g sucrose were dissolved in this mixture with the aid of gentle heat (the temperature was maintained below 50). The resulting solution was transferred to a separator with the aid of 5 ml 5M ammonia solution and 10 ml ethanol (96%v/v) and extracted with 20 ml chloroform and then with 2 x 30 ml of a 3 : 1 mixture of chloroform and ethanol. Each chloroform fraction, after separation, was washed, by gentle agitation, with the same 12 ml of a 3 : 1 mixture of water and ethanol. The combined chloroform fractions were evaporated to dryness and the residue dissolved, as completely as possible, in 10 ml calcium hydroxide solution using gentle heat. The solution was cooled and filtered into a separator, and the process repeated with a further 10 ml and 5 ml calcium hydroxide solution using the same filter as before. The combined calcium hydroxide solutions were extracted with 2 x 10 ml chloroform, and the combined chloroform fractions were washed with 10 ml water. The chloroform was discarded and to the combined aqueous fractions were added 10 ml M HCl, and the whole was extracted with a further 2 x 10 ml chloroform. The combined chloroform fractions were washed with 10 ml water and the chloroform discarded. The combined aqueous layers were heated on a water-bath to remove any residual chloroform, cooled and made to 100 ml with water. To 20.0 ml of a filtered portion of this solution were added 8 ml of a freshly prepared 1.0%w/v solution of sodium nitrite and the method continued as for the determination of anhydrous morphine in the monograph for chloroform and morphine tincture (British Pharmacopoeia 1980b) commencing at the words: '... allow to stand in the dark for fifteen minutes ...'. Anhydrous morphine contents are given in Table 1; replicate determinations were performed on all samples. Samples (i)-(iii) were prepared from opium tinctures with known anhydrous morphine contents and gave the recoveries of anhydrous morphine as indicated. Because of possible interference from other components of the mixture, aromatic chalk with opium mixtures were prepared to the British Pharmacopoeia (1980a) formulation but omitting the opium tincture. When these were assayed by the described method, the result was an apparent anhydrous morphine content of -0.001 to +0.002%. This compares favourably with an apparent anhydrous morphine content of ±0.001% obtained as a background reading when 20 ml portions of 0.1M HCl were assayed by the described method commencing at the addition of sodium nitrite solution. Suitable limits for the content of anhydrous morphine in aromatic chalk with opium mixture B.P. would be 0.045 - 0.055%w/v.

Table 1: Anhydrous morphine content of aromatic chalk with opium mixture B.P.

Sample	Anhydrous morphine content (%w/v)	% recovery of morphine
(i)	Mean 0.054 Range 0.052-0.054 n = 4	102.9
(ii)	Mean 0.052 Range 0.051-0.054 n = 4	99.0
(iii)	Mean 0.053 Range 0.052-0.054 n = 3	101.9

British Pharmacopoeia (1980a) H.M.S.O. London, p687
British Pharmacopoeia (1980b) Ibid. p834