Table 4. Determination of SA in commercial ASA (raw material and solid pharmaceutical forms). Results are compared with the official U.S.P. XIX procedure.

Type of sample	Sample concn. (mg ml^{-1})	% SA added (mg ml^{-1})	% SA found	% SA U.S.P. method
Commercial ASA	1·5	0·0015	0·11	0·12
Commercial ASA	1·5	0·0015	0·084	0·081
Tablets	3·0	0·003	0·014	0·014
Tablets	3·0	0·003	0·016	0·016
Tablets	3·0	0·003	0·016	0·017
Tablets (microincapsulated ASA)	0·3	0·0015	0·58	0·56
Tablets (microincapsulated ASA)	0·3	0·0015	0·38	0·40
Tablets (microincapsulated ASA)	0·3	0·003	0·48	0·45

be avoided and results can be given with a high degree of accuracy and precision; furthermore no calibration curve is needed. Rather than the more usual technique based on a comparison between the second derivative spectrum of a standard solution and that of the sample, the method reported in this paper is based on the comparison of the sample solution with a reference solution containing the same substances of the sample and not only the reference product. This procedure is less time-consuming and has the same degree of accuracy and precision.

The solvent used for the determination, besides having the capacity to avoid hydrolytical degradation of ASA, shows a low volatility and good solvent properties for common excipients. It is, nevertheless, advisable to complete the determination in the minimum amount of time required for this procedure to reduce the time of solvent–solute interaction.

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Determination of the anhydrous morphine content of ammonium chloride and morphine mixture B.P.

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The British Pharmacopoeial assay for the content of anhydrous morphine in ammonium chloride and morphine mixture (mistura tussi sedetiva) depends upon liquid–liquid extraction followed by colour development with nickel chloride/iodic acid reagent. This method is unsatisfactory in that it takes about 6 h to perform and produces inconsistent results (Table 1). It does, however, overcome the problem of interference from the liquorice content of the mixture, which, until recently, had prevented the application of the Radulescu type determination to liquorice containing pharmacopoeial morphine preparations (Helliwell & Sanders 1978; Helliwell & Game 1980).

A procedure is now described which overcomes this interference and allows the determination of the morphine content of ammonium chloride and morphine mixture by the method of Radulescu (1905) as modified by Adamson & Handisyde (1946). For this, four samples of the mixture were examined; one was a laboratory prepared sample and the other three were purchased from local pharmacies. The laboratory sample and one of the purchased samples were prepared from the components of the mixture, whilst the other two purchased samples were prepared by diluting commercially available concentrates.

The anhydrous morphine content was determined by the following method:

20·0 g sucrose were dissolved in 15·0 ml of the preparation with the aid of gentle heat (the temperature was maintained below 40 °C). This solution was transferred to a separator with the aid of 3 ml dilute ammonia solution (10% w/w) and 5 ml ethanol (96% v/v). The mixture was extracted with 20 ml chloroform and then with 2 × 20 ml of a 4:1 mixture of chloroform and ethanol. Each chloroform fraction, after separation, was washed, by *gentle* agitation, with the same 2 × 12 ml of a 3:1 mixture of water and ethanol. The combined chloroform fractions were evaporated to dryness on a waterbath and 5 ml M HCl added with gentle warming to dissolve the residue as completely as possible. This acid extract was transferred to a 50 ml volumetric flask with the aid of water and made to volume. 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 in water. This mixture was allowed to stand

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Table 1. Results from replicate assays for the anhydrous morphine content of ammonium chloride and morphine mixture B.P.

Sample	Anhydrous morphine content by proposed method (% w/v)		Anhydrous morphine content by B.P. 1980 method (% w/v)	
(i)	Mean	0·0053	Mean	0·0048
	Range	0·0051–0·0053	Range	0·0045–0·0050
		n = 4		n = 4
(ii)	Mean	0·0052	Mean	0·0052
	Range	0·0053–0·0050	Range	0·0047–0·0058
		n = 5		n = 4
(iii)	Mean	0·0049		
	Range	0·0048–0·0050		n.d.
		n = 4		
(iv)	Mean	0·0052		
	Range	n = 3		n.d.

Key:
(i) Mixture made in the laboratory from individual components.
(ii) Mixture purchased from local pharmacy and made from individual components.
(iii) Mixture purchased from a local pharmacy and made from a commercially available concentrate.
(iv) Mixture purchased from a local pharmacy and made from a commercially available concentrate.
n.d. Not done.

in the dark for 15 min, after which 12 ml of dilute ammonia solution were added and the volume made to 50 ml with water. The extinction of a 4 cm layer of this solution was measured at the maximum at about 442 nm, using as a blank a solution prepared in the same manner and at the same time, but replacing the sodium nitrite solution with water. The content of anhydrous morphine was determined by reference to a calibration curve prepared from suitable portions of an accurately prepared 0·008% w/v solution of morphine in 0·1 M HCl, each being diluted to 20·0 ml with 0·1 M HCl and using the method described above commencing at the addition of sodium nitrite solution.

The anhydrous morphine contents of the samples examined are given in Table 1; replicate determinations were performed on all samples. Mixture (i) was prepared from a chloroform and morphine tincture with a known anhydrous morphine content and gave 100·9% recovery of anhydrous morphine.

The method described is simple, quantitatively reproducible (Table 1) and requires less than 90 min to perform. The present British Pharmacopoeial limits for content of anhydrous morphine in ammonium chloride and morphine mixture are 0·0040–0·0066% w/v and we suggest that with the improvement in accuracy and reproducibility of the proposed over the existing method these limits could be narrowed to 0·0045–0·0060% w/v anhydrous morphine content.

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Liposomes—A selective drug delivery system for the topical route of administration: gel dosage form

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Most research efforts with liposomes have been involved with the investigation of their use as drug carriers to particular target organs in either in vitro conditions or after oral or parenteral administration (Gregoriadis 1979; Papahadjopoulos 1979). Only one report (Mezei & Gulasekharam 1980) has related to the topical use of liposomes. In that study triamcinolone acetonide was encapsulated into liposomes and applied to rabbit skin in a 'lotion' form which provided a more favourable drug disposition than the conventional ointment. We have now tested the disposition of triamcinolone after topical application in liposomal and 'free' form incorporated in a hydrocolloid gel vehicle and applied to rabbit skin.

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Materials and methods

Preparation of liposomes: DL-α-Dipalmitoyl phosphatidylcholine, cholesterol (Sigma Chemical Company, St Louis, Mo.), and triamcinolone [2-^{14}C]acetonide (New England Nuclear, Boston, Mass.) (1·1:0·5:0·5 molar ratio) were dissolved in chloroform–methanol (2:1). The solvent was evaporated under vacuum until a smooth, dry lipid film was observed. Calcium chloride (8 mM) solution was added and the mixture was vigorously stirred for 10–20 min and then allowed to stand at room temperature (20 °C) for 1 h.