DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 10(3), 481-490 (1984)

STABILITY OF PANTHENOL,CHLORPHENESIN AND LIGNOCAINE IN SOLIDIFIED SODIUM STEARATE-BASED STICKS (SSSS).

Ali A.Kassem*,Amir G.Mattha**and Gaber K.El-Khatib*
*Faculty of Pharmacy,Cairo University,**Laboratory of Pharmaceutical Sciences,National Research Center,Dokki,Cairo,Egypt.

ABSTRACT.

The stability of Panthenol,Chlorphenesim and Lignocaine was determined in solidified sodium stearate-based sticks over an 18 months period.Panthenol was determined spectrophotometrically as pantonyl lactone,at 250 nm,after separation of any interfering substances on a double bed chromatographic column containing Dowex 50W-X4 resin on top of Amberlite G400 resin. Chlorphenesin was determined spectrophotometrically at 280 nm wavelength after extraction with chloroform to separate any degradation products.Lignocaine was determined spectrophotometrically at 420 nm wavelength,as its Bromocresol green complex in chloroform,after extraction with the latter solvent from the solution of the stick in acid phthalate buffer at a pH of 4,2.

The obtained results pointed out to the very high stability of these drugs in the studied dosage form.This was mainly attributed to the high alcohol and low water contents of the sticks besides their thixotropic nature.

0363-9045/84/1003-0481$3.50/0

INTRODUCTION.

Two previous publications (1,2)threw light on the influence of three topically active drugs,Panthenol,Chlorphenesin and Lignocaine,on the physical characteristics and rheological properties of some solidified sodium stearate-based sticks in a study of the potentialities of these sticks as topical dosage form;among the main reasons having elicited such a topic were their high alcohol and low water contents and their solid structure,factors reputed to favour the stability of many drugs (3).However,in absence of any reports considering the stability of the three above mentioned drugs in such sticks,although reported to be stable in other dosage forms (4-7),it was imperative to study such an aspect of the formulation process; this being the purpose of the present work.

MATERIALS.

Solidified sodium stearate-based sticks containing 15% glycerol as humectant and 5% Panthenol,1% Chlorphenesin or 2% Lignocaine;these were prepared as mentioned in a previous publication (1).

Ion exchange resins: Dowex 50W-X4 (H^+ form),200-400 mesh and Amberlite G 400 (Cl^- form),type I,100-200 mesh.

Chloroform,A.R.;Bromochresol green (U.S.P.),0.21% aqueous solution;phthalate buffer (0.05M),pH 4.2:Sulfuric acid (98%), A.R.;absolute ethanol.

APPARATUS.

-Chromatographic ion-exchange column,double bed,filled with the ion-exchange resins mentioned above.

-Spectrophotometer,type SP6-400,Pye Unicam,Ltd.,Cambridge,

England,serial number 239185.

-Colorimeter,Carl Zeiss,Jena,made in G.D.R.,serial number 704982.

-Electric Centrifuge,type 5400,Model 194-337,Emil Dittemar and Vierth,Hamburg,West Germany,serial number,1993.

PROCEDURES.

Determination of Panthenol in the sticks:Several methods are available for the determination of Panthenol;these are either chemical (or physico-chemical)(8-13) or microbiological (14, 15).The method used in the present study was that proposed by Vachek (12);this involves heating the Panthenol solution in sulfuric acid (98%) to obtain Pantonyl lactone (152) which shows an absorption maximum at 260nm;the obtained absorption-concentration relationship obeys Beer's law up to a Panthenol concentration of 350 ug/ml.

Thus,8g of Panthenol stick was dissolved in water,adding a few drops of dilute hydrochloric acid and the volume completed with water to 250ml.The separated stearic acid was removed by filtration followed by thorough centrifugation of the filtrate;the filtrate was then eluted through a double bed chromatographic column (19 x 250mm)(16),prepared to consist of a 7cm length of Dowex 50W-X4 resin on top of 7cm height of Amberlite G 400 separated by a thin layer of glass wool.The packed column was prewashed with 1M hydrochloric acid then thouroughly washed with distilled water to avoid low recoveries and column-to-column variation (8);prior to packing the columns,the resins were soaked,individually,in water for several hours and slurried until most of the fines had been removed (16).The purpose of the ion-exchange resins was to remove the interfering substances as well as the hydrolysis products of Panthenol (16).

Accurately measured 25ml of the last elute was transferred to a 250ml volumetric flask and the volume adjusted with water.One milliliter of this solution was transferred to a test tube followed by 6ml of concentrated sulfuric acid;the mixture was shaken and heated on a boiling water bath for 30 minutes.After cooling to room temperature,the absorption of the solution at 260nm wavelength was measured on the UV-spectrophotometer against a blank prepared through the same steps using stick base without Panthenol.

Determination of Chlorphenesin in the Sticks:Several methods were reported for the determination of Chlorphenesin (6,17-20). The method adopted here depends on the extraction of the drug with chloroform from any of its degradation products(p-chlorophenoxylactic and p-chlorophenoxyacetic acids) (20)using the spectrophotometric method of determination (6,18)at 280nm wavelength.

Thus,8g of Chlorphenesin stick,accurately weighed,was dissolved in 100ml of water which had been rendered slightly acidic with a few drops of dilute hydrochloric acid.The precipitated stearic acid was separated by filtration.Twenty five milliliters of this filtrate was transferred into a 100 ml separating funnel and shaken thouroughly for 5 minutes with 20ml of chloroform before centrifugation at 2000 r.p.m. so as to effectively separate the organic layer.Ten milliliters of the chloroformic layer was pipetted into a suitable flask and the chloroform was evaporated completely on a water-bath at 65^{o}.The residue was dissolved in absolute ethanol and the solution transferred quantitatively into a 25ml volumetric flask where the volume was adjusted with absolute alcohol.Of this alcoholic solution,10ml was transferred into a 25ml volumetric flask,completed to volume with absolute alcohol,and the light absorbance of the sample measured at 280nm against a blank

prepared through the same steps using stick base without Chlorphenesin.

Determination of Lignocaine in the Sticks: Most official methods for Lignocaine determination depend mainly on the non-aqueous titration of the base or its salt (21-23); a spectrophotometric method was reported to estimate Lignocaine as a copper complex formed in alkaline medium (24). However, the most recent methods employ gas chromatographic techniques (25-27). A satisfactory, simple, specific and sensitive method, involving the use of Bromocresol green at an optimum pH of 4.2 to form a dye-Lignocaine complex showing maximum absorbance at 420 nm, was reported by E.Guergis (28); this method was adopted in the present work.

Thus, accurately weighed 8g of Lignocaine stick sample was dissolved in acid phthalate buffer solution (pH 4.2) and the precipitated stearic acid removed by filtration. The total volume of the filtrate was adjusted to 400ml; 25ml of this solution was transferred into a 200ml volumetric flask and the volume was adjusted with the buffer solution. A 2ml aliquot of this solution was pipetted into a 50ml separator, diluted with buffer (pH 4.2) to 7ml; 3ml of Bromocresol green solution was added and the separator contents were shaken with 20ml chloroform for 2 minutes and complete separation of the organic layer was effected in another 50ml separator containing 5ml of water and shaken touroughly for 2 minutes. Complete separation was allowed before centrifugation for 2 minutes at 2000 r.p.m. was made to effectively separate the organic washed chloroformic acid-dye complex (28). The absorbance of this complex was measured at 420nm against a blank prepared through the same steps using stick base without Lignocaine.

The concentrations of the drugs in the sticks were determined using preconstructed calibration curves prepared from

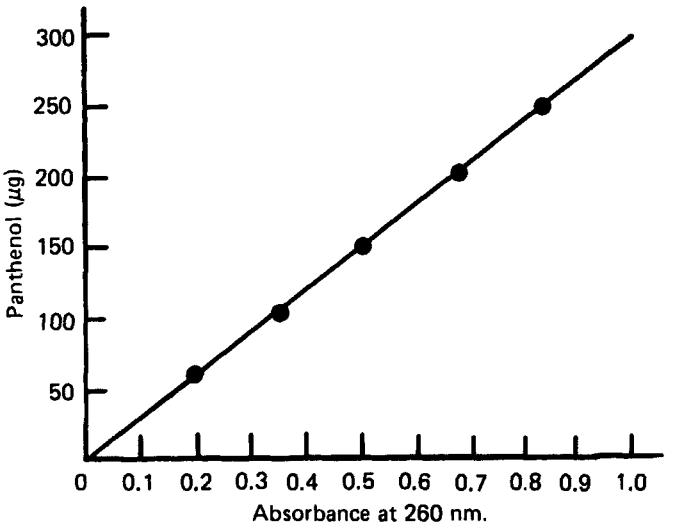

FIGURE 1
Calibration Curve of Panthenol.

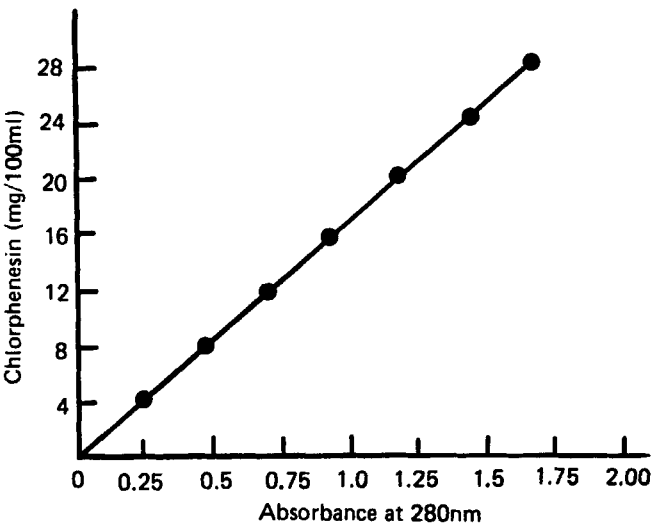

FIGURE 2
Calibration Curve of Chlorphenesin.

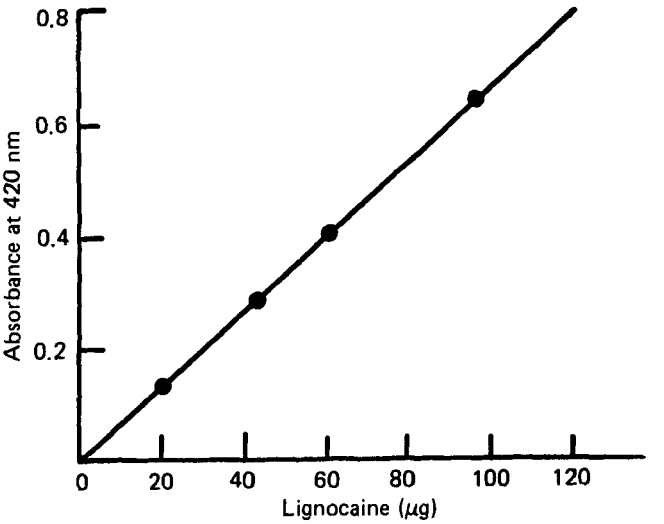

FIGURE 3
Calibration Curve of Lignocaine.

TABLE 1
Percent Stability of Panthenol, Chlorphenesin and Lignocaine in Solidified Sodium Stearate-based Sticks, Along an 18 Months Period.

	Percent Stability of the Medicaments				
	Fresh	After 3 Months	After 6 Months	After 12 Months	After 18 Months
Panthenol	100.0	99.9	99.5	98.8	99.0
Chlorphenesin	100.0	100.0	100.6	100.6	101.0
Lignocaine	100.0	100.0	100.0	100.7	100.7

standard aqueous solutions of the drugs and subjected to the same steps described above(figures 1-3).

Determinations were carried out right after preparation then after 3,6,12 and 18 months.During this period,the sticks were kept in tightly closed containers at ambient room temperature.

RESULTS AND DISCUSSION.

Table 1 shows that the three investigated medicaments, Panthenol,Chlorphenesin and Lignocaine are highly stable in SSSS dosage form,over the 18 months storage period.The thixotropic nature of these sticks (2) surely contributes to keep the incorporated medicaments stable (29).Moreover,the high alcohol content of the sticks might have offered optimal conditions to the stability of the medicaments,especially in presence of a very low water content.

CONCLUSIONS.

The obtained results favour the use of this type of vehicle in which one or more of the selected medicaments may be incorporated for topical application purposes with excellent prediction of shelf-life stability of the incorporated medicaments.

REFERENCES.

1.A.A.Kassem,A.G.Mattha and G.K.El-Khatib,Drug Development and Industrial Pharmacy

2.A.G.Mattha,A.A.Kassem and G.K.El-Khatib,Drug Development and Industrial Pharmacy

3.A.A.Kassem,A.G.Mattha and G.K.El-Khatib,Int.J.Cosmet.Sci., under publication.

4.S.H.Rubin,L.Magid ang J.Scheiner,Drug Cosmet.Ind.,86,42,10 (1960).

5.B.Idson,Drug Cosmet.Ind.,114,36,114(1974).

6.P.Stross and R.E.Stuckey,J.Pharm.Pharmacol.,2,549(1950).

7.C.Sung and A.Trwant,J.Pharmacol.Exp.Ther.,112,432(1954).

8.M.Hashmi,"Assay of Vitamins in Pharmaceutical Preparations John Wiley and Sons,London,1973,p.123.

9.R.G.Panier and J.H.Close,J.pharm.Sci.,53,108(1964).

10.E.G.Wollish and M.Schmall,Analytical Chem.,22,1033(1950).

11.M.Schmall and E.G.Wollish,Analytical Chem.29,1509(1957).

12.J.Vachek,Pharmazie,21,222(1966).

13.A.R.Prosser and A.J.Sheppard,J.pharm.Sci.,58,718(1969).

14.O.D.Bird and L.McCready,Analytical Chem.,30,2045(1958).

15.C.G.Rogers and J.H.Campbell,Analytical Chem.,32,1662(1960)

16.A.F.Zappala and C.A.Simpson,J.pharm.Sci.,50,845(1961).

17.British Pharmacopoea,The Pharmaceutical Press,London,1973.

18.British Pharmaceutical Codex, The Pharmaceutical Press,London,1979,p.181.

19.A.A.Forist and R.W.Judy,J.pharm.Sci.,53,1244(1964).

20.J.F.Douglas,J.A.Stockage and N.B.Smith,J.pharm.Sci.,59,107 (1970).

21.European Pharmacopoea,Vol.II,Maisonneuve,S.A.,p.293.

22.United States Pharmacopoea,XIX,Mack Publishing Company,Easton Pennsylvania,U.S.A.,1975.p.283.

23.British Pharmaceutical Codex,The Pharmaceutical Press,London,1973,p.701.

24.J.F.De Freitas,Aust.Dent.J.,22,182(1977).

25.T.R.Irgens,W.M.Henderson and W.H.Shelber,J.pharm.Sci.,65, 608(1976).

26.H.B.Hucker and S.C.Stauffer,J.pharm.Sci.,65,925(1976).

27.G.Caille,J.Leborier,Y.Latour and J.G.Besner,J.pharm.Sci., 66,1383(1977).

28.E.H.Guergis and S.Mahmoud,Can.J.Pharm.Sci.,14,24(1977).

29.G.D.Chase,in "Remington's Pharmaceutical Sciences",,J.E.Hoover,ed.,Mack Publishing Company,Pa.,U.S.A.,1970,p.365.