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Simultaneous Estimation of Halobetasol Propionate and Salicylic Acid by RP- HPLC Method

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ABSTRACT

An HPLC method for simultaneous estimation of halobetasol propionate and salicylic acid was developed using SS wakosil II. C18, 250 X 4.6 mm, 5 µm column. With mobile phase composition of methanol, buffer (55:45) flow rate of 1 ml/min and UV detection at 263 nm linearity was observed over the concentration range of 20-80 ppm for halobetasol propionate and 20-80 ppm for salicylic acid. The accuracy of the proposed method was determined by recovery studies and found to be 99.8% for halobetasol propionate and 99.46% for salicylic acid the proposed method was validated and results confirmed with the ICH parameters.

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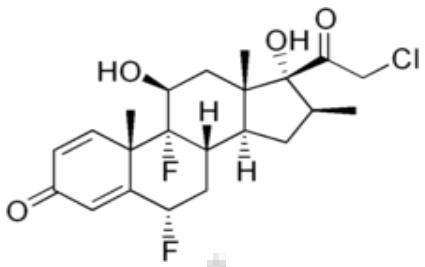
INTRODUCTION

DRUG PROFILE

Halobetasol Propionate

Structure:



Chemical Formula: $C_{22}H_{27}ClF_2O_4$

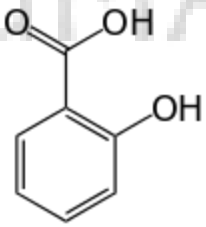
Molecular Weight: 428.897g/mol

IUPAC: (6α,11β,16β)-21-chloro-6,9-difluoro-11,17-dihydroxy-16-methylpregna-1,4-diene-3,20-dione

DRUG PROFILE

Salicylic Acid

Structure:



Chemical formula: $C_7H_6O_3$

Molecular Weight: 138.12 $g \cdot mol^{-1}$

IUPAC: 2-Hydroxybenzoic acid

Category: Antifungal Agents

Description: This compound belongs to the class of organic compounds known as salicylic acids. These are ortho-hydroxylated benzoic acids.

Pharmacodynamics

Salicylic acid treats acne by causing skin cells to slough off more readily, preventing pores from clogging up. This effect on skin cells also makes salicylic acid an active ingredient in several shampoos meant to treat dandruff. Use of straight salicylic solution may cause hyperpigmentation on unpretreated skin for those with darker skin types (Fitzpatrick phototypes IV, V, VI), as well as with the lack of use of a broad spectrum sunblock. Subsalicylate in combination with bismuth form the popular stomach relief aid known commonly as Pepto-Bismol. When combined the two key ingredients help to control diarrhea, nausea, heartburn, and even gas. It is also very mild antibiotic.

Mechanism of Action

Salicylic acid directly and irreversibly inhibits the activity of both types of cyclooxygenases (COX-1 and COX-2) to decrease the formation of precursors of prostaglandins and thromboxanes from arachidonic acid. Salicylate may competitively inhibit prostaglandin formation. Salicylate's antirheumatic (nonsteroidal anti-inflammatory) actions are a result of its analgesic and anti-inflammatory mechanisms. Salicylic acid is a key ingredient in many skincare products for the treatment of acne, psoriasis, calluses, corns, keratosis pilaris, and warts. It works by causing the cells of the epidermis to slough off more readily, preventing pores from clogging up, and allowing room for new cell growth. Because of its effect on skin cells, salicylic acid is used in several shampoos used to treat dandruff. Salicylic acid is also used as an active ingredient in gels which remove verrucas (plantar warts). Salicylic acid inhibits the oxidation of uridine-5-diphosphoglucose (UDPG) competitively with nicotinamide adenosine dinucleotide (NAD) and noncompetitively with UDPG. It also competitively inhibits the transferring of glucuronyl group of uridine-5-phosphoglucuronic acid (UDPGA) to the phenolic acceptor. The wound-healing retardation action of salicylates is probably due mainly to its inhibitory action on mucopolysaccharide synthesis.

MATERIALS AND METHODS

1. Chemical And Reagents

Water of HPLC grade was collected from a Milli-Q system. Potassium dihydrogen phosphate AR (Ranbaxy) orthophosphoric acid AR (Ranbaxy) mobile phase were purchased from the market.

2. Apparatus and Chromatographic Conditions

A gradient high pressure liquid chromatograph Shimadzu 10AT, SPD 10A detector was used for study. The column used was a reverse phase SS wakosil II, C18, 250 x 4.6 mm, 5 mm i.d and Particle size 5 µm. The flow rate of mobile phase was maintained at 1 ml/min and detection was carried out at 263nm at the room temp.

3. Preparation of Mobil Phase

A mixture of methanol and 0.02 M potassium dihydrogen phosphate buffer (adjust in the ratio of 75:25 v/v was filtered through 0.45 µ membrane filter was used as mobile phase. and sonicated for 10 min.

Mobile Phase: Degassed Methanol and Buffer in the ratio of 55:45 V/V.

Preparation of (KH_2PO_4 0.1M) buffer: Weight 3.8954g of di-sodium hydrogen phosphate and 3.4023 of potassium dihydrogen phosphate into a beaker containing 1000 ml of distilled water and dissolved completely. Then pH is adjusted with orthophosphoric acid and then filtered through 0.45 µm membrane filter.

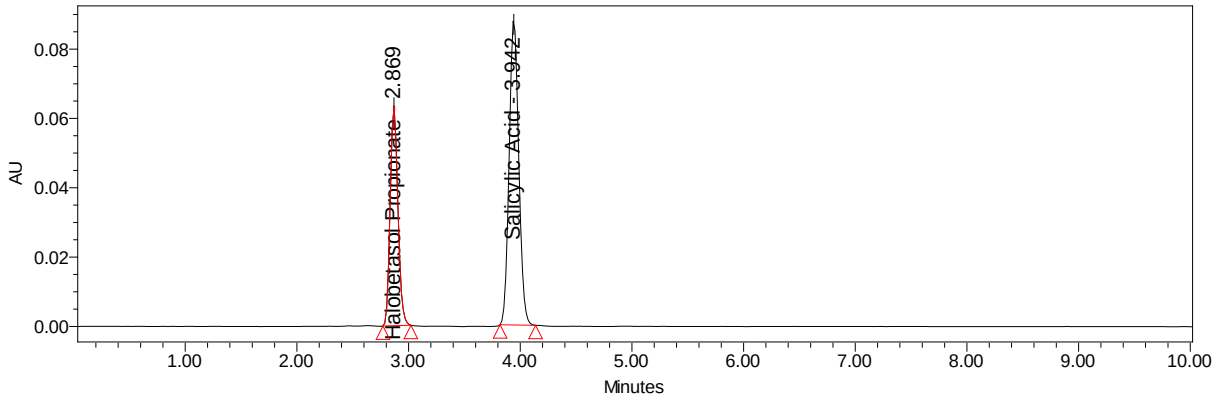
Preparation of stock solution:

Reference solution: The solution was prepared by dissolving 20.0mg of accurately weighed Halobetasol Propionate and 25.0mg Salicylic Acid in Mobile phase, in two 100.0mL volumetric flasks separately and sonicated for 20min. From the above solutions take 10.0mL from each solution into a 50.0mL volumetric flask and then make up with mobile phase and sonicated for 10min.

Preparation of working standard solution:

The stock solutions equivalent to 20ppm to 80ppm with respect to both drugs were prepared in combination of Halobetasol Propionate and Salicylic Acid above, sonicated and filtered through 0.45 µ membrane.

Chromatogram of sample solution



RESULTS FOR SYSTEM SUITABILITY OF HALOBETASOL PROPIONATE

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	2.869	797564	8676.113795	1.099100
2	2.867	795138	8803.641669	1.103929
3	2.871	795685	8616.937115	1.111477
4	2.868	800569	8820.182543	1.117660
5	2.872	797049	8735.115629	1.119004
Mean	2.869241	797201	8730.398	1.110234
SD	0.002683	2124.413	-------	-------
% RSD	0.064022	0.266484	-------	-------

RESULTS FOR SYSTEM SUITABILITY OF SALICYLIC ACID

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	3.942	1139272	5890.964069	1.238915
2	3.942	1140892	5915.423628	1.230637
3	3.944	1136301	5934.796986	1.240858
4	3.940	1141067	5976.253744	1.238995
5	3.943	1136024	5953.814152	1.241073
Mean	3.943118	1138711	5934.251	1.236496
SD	0.000837	57540.015	-------	-------
% RSD	0.028363	0.213538	-------	-------

The proposed method was validated as per ICH parameters. Precision of the proposed HPLC method was carried out by injecting replicate of six of concentration 20ppm and the precision of the proposed HPLC method was found to be 0.44% for halobetasol propionate and 0.93% RSD for salicylic acid. The low RSD values indicated that the proposed method had good precision.the precision of instrument was carried out by injecting replicate of six of concentration 20ppm. The precision of the instrument was found to be 0.50% for halobetasol propionate and 0.43% RSD for salicylic acid. Accuracy of the method was determined. The average recovery of halobetasol propionate were 99.8% and for salicylic acid 99.46% respectively. The sample recovery in the formulation was in good agreement with the label claim. High percentage recovery showed that the method was free from interferences of the excipients used in the formulations. Ruggedness of the method was determined by carrying out the assay by different analyst on different days. The test result was found to be satisfactory with RSD for set of analysis on the same date being less than 0.8% and RSD between set of analysis on different days being less than 1.6% for both halobetasol propionate and salicylic acid. The percentage area on calculation was found to be 101-102% for halobetasol propionate and 99-101% for salicylic acid. This shows that the result is reproducible. Robustness of the method was determined by carrying out the assay during which the mobile phase ratio and pH of mobile phase were altered slightly. The percentage recovery was found to be 99.8% for halobetasol propionate and 99.46% for salicylic acid. When mobile phase was altered slightly. System suitability parameters of

halobetasol propionate and salicylic acid were given in the tables. Assay of the combination in tablet dosage form was found to be 94.5% of halobetasol propionate and 105.6% of the salicylic acid.

CONCLUSION

The method was simple and had short runtime of 4 min, which make the method rapid. The results of the study indicate that the proposed HPLC method was simple, precise, highly accurate specific, and less time consuming.

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