Організація наукових медичних досліджень «Salutem»

ЗБІРНИК МАТЕРІАЛІВ

МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ КОНФЕРЕНЦІЇ

«ФАРМАЦЕВТИЧНІ ТА МЕДИЧНІ НАУКИ: АКТУАЛЬНІ ПИТАННЯ»

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Ф24 **Фармацевтичні та медичні науки: актуальні питання:** збірник матеріалів міжнародної науково-практичної конференції (м. Дніпро, 9–10 квітня 2021 р.). – Дніпро : Організація наукових медичних досліджень «Salutem», 2021. – 72 с.

У збірнику представлені матеріали міжнародної науково-практичної конференції **«Фармацевтичні та медичні науки: актуальні питання»**. Розглядаються загальні проблеми клінічної та профілактичної медицини, питання фармацевтичної науки та інше.

Призначений для науковців, практиків, викладачів, аспірантів і студентів медичної, фармацевтичної та ветеринарної спеціальностей, а також для широкого кола читачів.

Усі матеріали подаються в авторській редакції.

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НАПРЯМ 4. ФАРМАЦЕВТИЧНА НАУКА: СУЧАСНІСТЬ ТА МАЙБУТНЄ

НАПРЯМ 4. ФАРМАЦЕВТИЧНА НАУКА: СУЧАСНІСТЬ ТА МАЙБУТНЄ

TITRIMETRIC MICRO-DETERMINATION OF HYDROXYZINE USING OXONE

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Hydroxyzine dihydrochloride (HDH) [2192-20-3], chemically known as (RS)-2-{2-[4-(p-chlorophenylbenzyl)piperazin-1-yl]ethoxy}ethanol dihydrochloride (Fig. 1), is the first-generation antihistamine of the piperazine class that is an H_1 receptor antagonist, that exhibits sedative, anxiolytic, and antiemetic properties [1, 2].

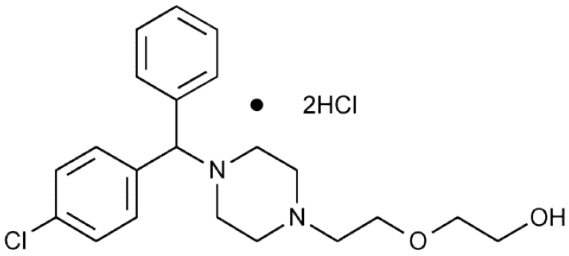

Fig. 1 Chemical Formula of Hydroxyzine Dihydrochloride

Drug substance Hydroxyzine Hydrochloride is monographed in the PH (Ph Eur., BP 2018, USP 41).

The pharmacopoeia method is based on the potentiometric titration of HDH in non-aqueous medium using perchloric acid [3].

The official USP method which is also available for the assay of the drug in tablets employs a chromatographic system equipped with a UV-detection, where HDH can be detected at 232 nm [4].

Determination of HDH in pharmaceutical preparations is important for pharmaceutical needs, and hence it is crucial to develop simple, sensitive, selective, and cost-effective methods for its determination as a part of compliance of specifications study: specimen quantity, sample homogeneity, and content uniformity in tablets.

Different methods have been used for the determination of the antihistaminic drug HDH including HPLC [5], GC [6], spectrophotometry [7], potentiometry [8], voltammetry [9], capillary zone electrophoresis using chiral selectors [10] and titrimetry.

So, a titrimetric assay of some antihistamines through the determination of the chloride of their hydrochlorides has been reported. The chloride content of the drug is determined by titration with mercury (II) using diphenylcarbazone-BTB as indicator [11]. Two simple titrimetric methods have been developed for the determination of hydroxyzine dihydrochloride (HDH) in pure form and in tablets. The principle of the methods are simple acid-base reactions in which the hydrochloride content of the drug was determined by titrating with an aqueous standardized NaOH solution either visually using phenolphthalein as indicator (method A) or

potentiometrically (method B) using glass-calomel electrode system. The methods were applicable over the range of 2-20 mg HDH. The procedures were also applied for the determination of HDH in its dosage forms and the results were found in good agreement with those obtained by the reference method [12]. Two simple, rapid, reliable, precise and accurate and cost-effective non-aqueous titrimetric procedures have been developed for the determination of hydroxyzine dihydrochloride (HDH) in bulk drug and its pharmaceutical formulations. The methods are based on the titration of the drug in glacial acetic acid in the presence of mercuric acetate with acetous perchloric acid to the visual end point using crystal violet as indicator [13].

An inspection of most of the available methods for the above mentioned drug reveals that most of them are either cumbersome or time consuming, or involve the use of expensive equipment and reagents. On the other hand, titrimetry is the simplest analytical techniques extensively used in the drug standardization laboratories. Redox titrimetry may serve as useful alternative to many of the aforesaid sophisticated techniques because of their cost effectiveness, ease of operation, sensitivity, remarkable accuracy and precision, and wide applicability.

The present investigation aims to develop simple, sensitive, and cost-effective method for the determination of HDH in pure form and tablets using redox titrimetric technique. The method involves the use of potassium hydrogenperoxomonosulphate ($KHSO_5$, PMS) in form oxone (the triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) as the titrant. A known excess of reagent is added and, after a specified time, the residual reagent is determined iodometrically. The procedure have several advantages, such as speed, simplicity, accuracy and precision, selectivity and cost-effectiveness, and consequently, it can be easily adapted by the quality control laboratories for the routine analysis.

In the present investigation, PMS was found to react quantitatively with HDH in alkali medium to form the N-oxide. A stoichiometry of the reaction between PMS and HDH showed that for oxidation of 1 mol HDH 1 mol of PMS were required. The relationship between the titration end-points obtained by the proposed method and the HDH amounts was examined. The linearity between the amount of HDH and titration end-point is apparent from the correlation

coefficient. The correlation coefficient of 0.999 show that the reaction between PMS and the studied HDH proceeds stoichiometrically and quantitatively. To prove the validity and applicability of the proposed method, four replicate determinations at different concentration levels of HDH was carried out. The within-day RSD values were within 2%.

The scheme of *N*-oxidation of hydroxyzine with potassium hydrogenperoxomonosulphate is shown in Fig. 2.

The method was successfully applied to the assay of HDH in tablet formulation «Atarax» with Hydroxyzine hydrochloride on 25 mg; Manufacturer: YUSB Pharma S.A. (USB Pharma, S.A.) (Belgium), Thyssen Laboratories (Laboratories Thissen) (Belgium) and the results were statistically compared with those of a reference method. No interference was observed from common tablet adjuvants. The accuracy and reliability of the methods were further ascertained by recovery experiments via the standard-addition technique. Results with a recovery of 99.5 % and a mean standard deviations of ±1.3 % of the nominal are obtained which compared fairly well with data obtained using the British pharmacopoeia method.

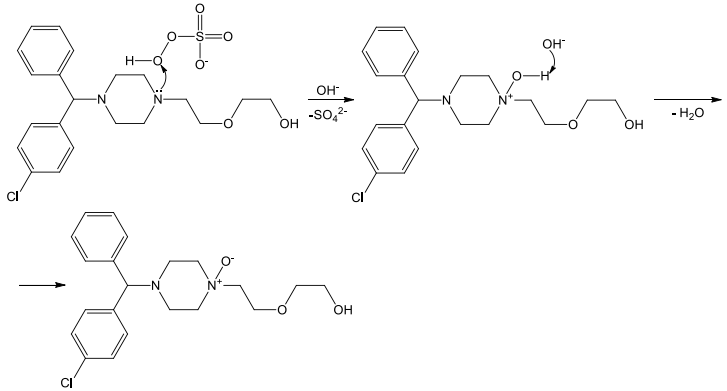

Fig. 2. Scheme of *N*-oxidation of Hydroxyzine with potassium hydrogenperoxomonosulphate

Conclusion. The reported methods (HPLC) suffer from such drawbacks as high cost, multiple steps and also several clean-up steps. They are time consuming and require organic toxic solvents.

Any method chosen for the routine analysis should be reasonably simple, used materials should readily be available in the laboratory or readily obtainable and require a minimum amount of the equipment. These objectives have been fulfilled by the titrimetric procedure developed. The accuracy, reproducibility, simplicity and cost-effectiveness of the method suggest their application in the quality control laboratories where the modern and expensive instruments are not available.

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СПОСОБ ПРЕДУПРЕДИТЬ ОСЛОЖНЕНИЯ ПРИ COVID-19 У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ 2 ТИПА

СКАЧКО Б. Г.
врач-фитотерапевт
ТОВ клуб «Здоров-е»
г. Киев, Украина

Изменения в сосудах при сахарном диабете находятся в прямой зависимости от степени компенсации углеводного обмена. Повышение гликозидированного гемоглобина от 6,5% на 1% почти в 2 раза увеличивает риск развития микроангиопатии (1). А при исходном уровне гликозидированного гемоглобина 7% повышение на 1%

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