Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1443-1446 | ISSN:2251-6727

Spectrophotometric Determination of Tetrahydrocurcumin using Sulfa Drugs as Coupling Reagents

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(Received: 27 October 2023 Revised: 22 November Accepted: 26 December)

KEYWORDS
tetrahydrocurcumin
diazotization
sulfanilamide
sulfadoxine,
sulfamethxazole
spectrophotometry

ABSTRACT:

Tetrahydrocurcumin (THC), is a cosmeceutical which is colourless and is reduced form of yellow curcuminoids extracted from the roots of Curcuma longa, commonly called turmeric. A study was made of the application of diazotization-coupling spectrophotometric technique for the determination of tetrahydrocurcumin, using sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) - the widely used sulfa drugs as coupling agents. The methods are based on the interaction of diazotized drugs with THC in alkaline medium to produce a red colour product having maximum absorption at 500 nm. The colour developed was stable for 6 h at 27°C. Beer's law was obeyed in the concentration range 1.0-14.0 ug ml^{-1} for SAA and SMX and 2.0-16.0 ug ml^{-1} for SDX at the wavelength of maximum absorption at 500 nm. The method was also successfully tried for the determination of THC in presence of common excipients used as additives, which did not interfere in the proposed methods. **Introduction**: In recent years, there is a resurgence globally for alternate medicines where the people who obtained health care from physicians, pharmacists and other professionals needed to be supported by safe and cost effective and more accessible health products. It is in this delicate balance of health care and surge for alternate medicine, the field of "nutraceuticals" emerges.

Objectives This paper is an attempt to meet an ever-increasing demand for the analytical control of commercialized health care products by developing simple, sensitive, selective, rapid and reliable spectrophotometrie procedures for the determination of the newly introduced cosmeceutical product. Survey of literature revealed that no analytical method has been developed so far for the determination of the THC using sulfanilamides as spectrophotometric reagents.

Methods: The methods involve coupling of diazotized sulfanilamides with tetrahydrocurcumin in alkaline medium to produce red colour. The proposed methods have distinct advantages of sensitivity and stability. Besides, the methods do not require heating or distillation and exhibit reliability due to reproducibility.

Results: A red coloured product with maximum absorption at 500 mm was formed when sulfanilamide, sulfadoxine, sulfamethoxazole reacted with tetrahydrocurcumin in sodium hydroxide medium.

Conclusions: The herbal renaissance has produced a profound effect on the Western medical system, which is now trying to acknowledge methods of healing that was in existence for millennia in the traditional medicine throughout the world, especially Asia. The surge in research on drugs from natural sources is now moving out of the herbalists shop away from the core texts into the drugs research laboratories. With increasing consumer awareness, the pharmaceutical industries in drug control authority have long been interested in the development of simple and sensitive methods for the assay and evaluation of drugs in bulk and in dosage forms, to assure high standard in quality control. In the present context, determination or estimation of cosmeceuticals is of paramount importance. Simple methods based on spectrophotometry may dominate as analytical tool for the evaluation of cosmeceuticals. Our methods are a step forward towards this direction. The proposed spectrophotometric methods have adequate sensitivity and accuracy for determination of tetrahydrocurcumin. Their analytical characteristics such as sensitivity, selectivity and stability are far superior to other existing spectrophotometric methods.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1443-1446 | ISSN:2251-6727

1. Introduction

Sulfanilamides which are commonly used as antibacterials are aniline substituted sulfonamides. Though, a large number of synthesized sulfanilamide derivatives are reported in the literature, only about two dozen of them have been used in clinical practice [1]. Even in spite of the toxicity shown for some patients and sulfanilamide-resistant bacterial strains the use of these drugs in combination, especially sulfonamide-trimethoprims is extensively used to control opportunistic infections in patients with AIDS, pneumonia (Pneumocystis carinii) treatment and prophylaxis, cerebral toxoplasmosis treatment and prophylaxis, urinary tract infections and burn therapy [2-4]. Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) are the chemicals which contain aromatic primary amino group. SDX is a long-acting sulfanilamide used in the treatment of various types of infections. It exhibits synergistic effect with pyrimethamine, which acts against folate metabolism at different points of the metabolic cycle. SMX is commonly used to treat uncomplicated urinary tract infection, more particularly those caused by Escherichia coli.

Nutraceuticals encompass a large group of preventive and curative health ingredients that have been predominantly derived from long standing medical tradition such as Ayurveda, Tibetian, Chinese and Japanese medical systems. All these systems primarily depend on plants, more commonly known as herbs, especially those with a well-established use as foodstuff. The blend of these pharmaceuticals and nutritional characteristics resulted in the name "nutraceuticals" to denote the nutritional origin and the design molded on pharmaceuticals, that is, standardization, efficacy and predictability. Cosmeceuticals are nutraceuticals which exhibit cosmetic properties.

Tetrahydrocurcumin (THC) is a cosmeceutical which is colourless and is a reduced form of yellow curcuminoids extracted from the roots of turmeric (Curcuma longa) [5]. Tetrahydrocurcumin exhibits strongest antioxidant activity among curcuminoids studied in several vitro systems [6,7]. It may therefore be used in colour - free foods and cosmetic products, which currently employ conventional synthetic antioxidants such as butylated hydroxytoluene. An antioxidant used in a cosmetic application should have the capability of efficiently quenching any radicals on the surface of the skin. Tetrahydrocurcumin has free-radical scavenging ability and skinlightening action [7]. It also displays anti-inflamatory [7] and anti-cancer activity [8]. Protective role of THC against erythromycin estolate induced hepatotoxicity has also been reported [9]. In recent communication we have reported the structural studies of THC [10]. The molecule is non-planar and the benzene rings positioned at the ends of heptane chain are orthogonally placed with a dihedral angle of 84.09(7) ° between them. The study was carried out to confirm the reports that the p-hydroxy functional groups are responsible for the antioxidant and chemopreventive action of the compound [11].

2.Objectives

This paper is an attempt to meet an ever-increasing demand for the analytical control of commercialized health care products by developing simple, sensitive, selective, rapid and reliable spectrophotometrie procedures for the determination of the newly introduced cosmeceutical product. Survey of literature revealed that no analytical method has been developed so far for the determination of the THC using sulfanilamides as spectrophotometric reagents. The methods involve coupling of diazotized sulfanilamides with tetrahydrocurcumin in alkaline medium to produce red colour. The proposed methods have distinct advantages of sensitivity and stability. Besides, the methods do not require heating or distillation and exhibit reliability due to reproducibility.

3.Methods

Apparatus

UV-VIS spectrophotometer UVIDEC-610 type with 1,0-em matched cell (Jasco, Tokyo, Japan) was employed for measuring the absorbance values

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Reagents

Tetrahydrocurcumin(THC) (Sami lab, India), sulfanilamide (SAA), sulfadoxine(SDX) and sulfamethoxazole(SMX) (Glaxo Smithkline Pharmaceuticals, India), sodium nitrite, suphamie acid and sodium hydroxide (Ranbaxy, India) were used. All other chemicals and solvents used were of analytical

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 1443-1446 | ISSN:2251-6727

reagent grade. Double distilled water was used throughout.

Tetrahydrocurcumin (100mg) was dissolved in isopropyl aleohol in a 100-ml volumetric flask and made up to the mark. The stock solution was further diluted with isopropyl alcohol to get solutions of required strength.
Aqueous solutions of 1.0% (w/v) sodium nitrite, 1.0% (w/v) sulphamic acid and 0.5N sodium hydroxide were prepared in distilled water. Aqueous solutions of 0.25% (w/v) sulfanilamide, sulfadoxine and sulfamethoxazole were prepared in distilled water.
Ten ml of 2N hydrochloric acid was added during the preparation of sulfadoxine and sulfamethoxazole to improve its solubility.

Procedures

Two ml each of SAA, SDX or SMX, and 1.0 ml each of sodium nitrite and sulphamic acid were transferred into a series of 25ml-calibrated flasks. Aliquots of standard solution of tetrahydrocurcumin were added to this and 1.0 ml of sodium hydroxide was added and the contents were shaken well, and diluted up to the mark using distilled water. The absorbance was then measured against the corresponding reagent blank at 500 mm. The details of the optical characteristics are shown in Table 1.

Table 1: Optical characteristics for the determination of tetrahydrocurcumin

Parameters	**SAA**	**SDX**	**SMX**
Colour	Red	Red	Red
λ (nm)	500	500	500
Stability (h)	6	6	6
Beer's law (µg ml^{-1})	1.0 – 14.0	2.0 – 16.0	1.0 – 14.0
Recommended concentration (µg ml^{-1})	9.0	10.0	9.0
Molar absorptivity (L mol^{-1} cm^{-1})	1.92 x 10^4	1.45 x 10^4	1.60 x 10^4
Sandell's sensitivity (µg cm^{-1})	0.019	0.025	0.023
Regression equation*			
Slope (a)	0.2402	0.1290	0.1760
Intercept (b)	0.0151	0.0042	-0.0091
Correlation coefficient	0.9869	0.9962	0.9998
R.S.D. % **	± 0.78	± 1.02	± 0.86

*y=ax+b where x is the concentration of tetrahydrocurcumin in µg ml^{-1}.
**relative standard deviation (n=5),
SAA: sulfanilamide, SDX: sulfadoxine,
SMX:sulfamethoxazole

4.Results

Optimization of analytical variables

The choice of an appropriate solvent/medium has profound influence on the sensitivity and reproducibility of the results. Full colour development and maximum sensitivity were achieved when the reaction was carried out in alkaline medium. It was found that sodium nitrite (1.0% w/v) in the range 0.5-3.0 ml, sulphamic acid (1.0% w/v) 0.5-2.5 ml and 0.5 N sodium hydroxide 0.5-2.5 ml gave reproducible results. Hence, sodium nitrite, sulphamic acid and sodium hydroxide each at 1.0 ml were recommended. Similar experiments were carried out to know the amount of SAA, SDX and SMX, It was found that 1.0-3.0 ml (0.25% w/v) of SAA, SDX and SMX were found to give maximum intensity, Hence, 2,0 ml of SAA, SDX and SMX were found appropriate,

Table I shows the linear calibration ranges and equation parameters for these methods. Separate determinations at different concentrations of each reagent gave a coefficient of variation not exceeding 2%,

Interference

The interference if any, by various substances was studied as per the procedure, It was found that excipients such as glucose, lactose, dextrose, starch, sodium alginate and sodium lauyrl sulphate did not interfere, while vitamin C was found to interfere (Table 2),

Table 2: Recovery of tetrahydrocurcumin in the presence of excipients and other substances using sulfanilamide

Material	Amount(mg)	% Recovery of tetrahydrocurcumin* ± RSD**

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JCHR (2024) 14(1), 1443-1446 | ISSN:2251-6727

Gluocose	50	97.2 ± 0.82
Lactose	50	100.3 ± 0.72
Dextrose	50	100.6 ± 1.02
Starch	50	99.8 ± 0.82
Sodium alginate	50	99.3 ± 0.89
Sodium lauryl sulphate	50	100.8 ± 1.04
Vitamin C	10	>50 < 60©

*9.0 µg ml^{-1} of tetrahydrocurcumin taken,**relative standard deviation (n=5), ©erratic values

5.Discussion

Weak electrophilic diazotized arylamines couple with strong activated substrates to give coloured azo dyes. When thesubstrates are also arylamines [12, 13], a weak acidic medium is recommended for coupling. But a basic medium is required with phenols, because only free amines and phenolate ions are sufficiently activated [14).

Unfortunately, unstable derivatives and large values of blank solutions are usually obtained. These effects are caused by the hydrolysis of dizonium ion of the reagent used for coupling to give a phenol in a process called hydroxy-de-diazotization [15] which reacts with excess of reagent in basic medium.

THC contains two hydroxyl groups and the proposed methods involve coupling of diazotized sulfa drugs with THC in basic medium to produce a red colour product with maximum absorption at 500 nm. The factors affecting the colour development such as reproducibility, sensitivity and adherence to Beer's law were investigated separately for each reagent

Refrences

I. Northey, E.H.The Sulfonamides and Allied Compounds.1948. ACS Monogr Ser American Chemical Society. Washington, DC .
2. Mandell G.L., Patri W.A. The Pharmacological Basis of Therapeutics.1996. Ed: A.G. Gilman, et al. 9" edition, New York, Macmillan
3. Jewetz E. Basic and Clinical Pharmacology. 1995.Ed: B.G. Katzung, 6* edition, Norwalk, CT, Appleton and Lange
4. FDA Drug Bulletin. Feb 1980. U.S. Department of Health, Education and Welfare. Food and Drug Administration.
5. Govindarajan V. S. 1980. Turmeric - Chemistry, technology and quality. CRC Crit. Rev. Food Sci. Nutr.12 , 199-301.
6. Osawa T., Sugiyama Y., Inayoshi M., Kawakishi S. 1995. Anti oxidantactivity of tetrahydrocurcuminoids. Biosci. Biotech. Biochem.. 59, 1609-1612.
7. Sugiyama Y., Kawakishi S., Osawa T.1996. Involvment of the ß-diketone moiety in the antioxidant mechanism of tetrahydrocurcumioids. Biochem. Pharmacol .52 , 519-525.
8. Nakamura Y. 1998.Inhibitory effect and tetrahydrocurcuminoids on the tumor promoter induced reactive oxygen species generation in leucocyte. Jpn. J Cancer. 89 ,361-370.
9. Pari L., Murugan P.2004. Protective role of tetrahydrocurcumin against erythromycin estolate-induced hepatotoxicity. Pharmacol. Res. 49, 481-486.
10. Girija C. R., Begum N. S. , Syed A. A.,Thiruvenkatam,V. 2004. Hydrogen-bonding and C- H …. Π interactions in 1,7-bis(4-hydroxy-3-methoxyphenyl)heptane-3, 5- dione (tetrahydrocurcumin). Acta Cryst. C60 , 0611-0613.
11. Rao T. S., Basu N., Siddiqui H. H.1982. Anti-inflammatory activity of curcumin analogues. Indian J Med Res. 75 , 574-578.
12. Schirmer R.E.1982. Modern Methods of Pharmaceutical Analysis. CRC Press, BocaRaton, FL. 1 ,83.
13. Norwitz G., Keliher P.N. 1981. Spectrophotometric determination of aniline by the diazotization-coupling method with 8-amino-1-hydroxynapthalene-3, 6-disulfonic acid as the coupling agent. Anal Chem.53, 56-60.
14. Baiocchi C., Gennaro M.C., Campi E., Mentasti E., Aruga R.1982.HPLC identification and separation of phenolic compounds diazotized with sulphanilic acid-Structural effects on retention times. Anal Lett 15 , 1539-1548.
15. March J.1992. Advanced Organic Chemistry.Wiley, New York.