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New Spectrophotometric Reagents for the Determination of Cardanol Based on Coupling with a Class of Sulfa Drugs

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Abstract

Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX), the widely used sulfa drugs are proposed as new coupling agents for the spectrophotometric determination of cardanol a phenolic compound found in cashew nut shell liquid which is a by-product of cashew industry. The methods are based on the interaction of diazotized sulfa drugs with cardanol to produce a yellow-coloured product with a maximum absorption at 415 nm. The colour developed was stable up to 24h. The methods obey Beer's law. The methods can be successfully employed for the determination of cardanol in presence of common excipients like glucose, lactose, dextrose, starch, sodium alginate and sodium lauryl sulphate, which do not interfere in the proposed methods.

***Key words*:** Cardanol, Diazotization, Sulfanilamide, Sulfadoxine, Sulfamethoxazole, Spectrophotometry

One of the frontiers of sustainable development is the utilization of agricultural by-products - a field of paramount importance in the domain of biodegradability and the use of agricultural waste and by-products, in place of toxic chemicals - an area of current interest in environmental management. Cardanol holds considerable promise because of its abundant availability in tropical areas, low cost, biodegradability [1] and structural characteristics [2]. Cardanol is commonly found in cashew nut shell liquid (CNSL), a by-product of cashew industry. CSNL is an alkyl phenol oil which constitutes 25% of the total weight of cashew nut (Anacardium occidentale) [3]. Cardanol (3-pentadecenyl phenol) is a phenolic compound with C15 aliphatic chains in the meta position. It is a mixture of saturated and unsaturated (mono, di- and tri-) compounds [4] The non-linear structure, unsaturation in the alkyl chain and substitution to phenolic group opens up new vistas in its innumerable applications including dyestuff, food, flavour, ion exchange resin, paints, plasticizers and polymers [5]. Significant studies have also been made in the technological applications of cardanol and its derivatives as pesticides [6], surface-active agents [6], in ceramics [2] and composites [11].

Sulfanilamides are commonly used as antibacterial that are aniline substituted sulfamides. Though, a large number of sulfanilamide derivatives synthesized are reported in the literature, only about two dozen have been used in clinical practice [7]. Despite the toxicity observed with some patients and the existence of sulfanilamide-resistant bacterial strains the use of these drugs in combination especially sulfonamide-trimethoprims has been extensively used for opportunistic infections in patients with AIDS, pneumonia (*Pneumocystiss carinil*) treatment and prophylaxis, cerebral toxoplasmosis treatment and prophylaxis, urinary tract infection and burn therapy [8-10]. 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*.

This paper is an attempt to develop simple, sensitive, rapid and reliable spectrophotometric methods for the determination of newly introduced agri by-product by exploring wide range of pharmaceuticals as new coupling agents. Survey of literature revealed that no sulfa drugs and their derivatives have been used for the spectrophotometric determination of cardanol. The methods reported here in involve coupling of diazotized sulfanimides with cardanol in alkaline medium to produce yellow 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.

MATERIALS AND METHODS

Experimental

Apparatus

UV-VIS spectrophotometer UVIDEC-610 type with 1.0-cm matched cell (Jasco, Tokyo, Japan) was employed for measuring the absorbance values.

Reagents

Cardanol (Vittal Mallya Scientific Research Foundation, India), sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) (Glaxo Smithkline Pharmaceuticals,

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India), sodium nitrite, suplhamic acid, sodium hydroxide (Ranbaxy, India) was used. All other chemicals and solvents used were of analytical reagent grade. Double distilled water was used throughout. Cardanol (100 mg) was dissolved in isopropyl alcohol 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 solutions 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 of SAA, SDX or SMX, 1.0ml each of sodium nitrite and sulphamic acid solution were transferred into a series of 25ml-calibratedflask. To this aliquot of standard solution of cardanol were added and 1.0 ml of sodium hydroxide was added and the contents were shaken well, and diluted to mark using distilled water. The absorbance was then measured against the corresponding reagent blank at 415 nm. The optical characteristics are shown in (Table 1).

Table 1 Optical characteristics for the determination of cardanol

Parameters	SAA	SDX	SMX
Colour	Yellow	Yellow	Yellow
λ (nm)	415	415	415
Stability (h)	24	24	24
Beer's law (μg ml^{-1})	1.0 – 14.0	2.5 – 30.0	1.0 – 13.0
Recommended concentration (μg ml^{-1})	7.0	14.0	7.0
Molar absorptivity (L mol^{-1} cm^{-1})	1.39 x 10^4	0.75 x 10^4	1.50 x 10^4
Sandell's sensitivity (μg cm^{-1})	0.020	0.038	0.019
Regression equation*			
Slope (a)	0.1322	0.1794	0.2401
Intercept (b)	0.0062	0.0023	0.0104
Correlation coefficient	0.9969	0.9876	0.9768
R.S.D. %**	± 0.90	± 1.09	± 0.67

*y= ax + b where x is the concentration of cardanol in μg ml^{-1}

**relative standard deviation (n=5)

SAA: sulfanilamide, SDX: sulfadoxine, SMX: sulfamethoxazole

RESULTS AND DISCUSSION

Aromatic diazonium ions couple with active substrates such as amines and phenols [11-13]. Because of the size of the attacking species, substitution is mostly para to the activating group. Unless that position is already occupied, in which case ortho substitution takes place. In case of cardanol, the substituent being in the meta position, the substitution is preferably in the para position. For the activation of the substrates pH of the media is of paramount importance. For phenols, alkaline medium is recommended because phenols themselves are not active enough for the diazotisation reaction. Nevertheless, there is a risk of unstable derivatives and large values of blank due to the process called hydroxy-de-diazonization [14] which reacts with excess of the reagent in basic medium.

The proposed sulfa drugs namely; Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) containing aryl primary amino group undergo diazotization reaction using sodium nitrite solution to produce diazonium group which reacts with cardanol in sodium hydroxide medium to produce a yellow colour dye. The method involves the coupling of the diazotized sulfa drug with cardanol to produce a yellow-coloured product with maximum absorption at 415 nm. The NH group of the sulfa drug gets readily diazotized during the diazotisation process to produce diazonium group which reacts with cardanol in sodium hydroxide medium to produce a yellow-coloured dye. The reproducibility, sensitivity and adherence too.

Spectral characteristics

A yellow-coloured product with maximum absorption at 415 nm was formed when sulfanilamide, sulfadoxine, sulfamethoxazole reacted with cardanol in sodium hydroxide medium.

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 an alkaline medium. It was found that sodium nitrite (1.0% w/v) in the range 0.5-2.5 ml, sulphamic acid (1.0% w/v) in the range 0.5-2.0 ml and 0.5 N sodium hydroxide 0.5-1.5 ml were sufficient to get reproducible results. Hence, sodium nitrite, sulphamic acid and sodium hydroxide each at 1.0 ml was recommended. Similar experiments were carried out to know the amount of Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX). It was found that 1.0-3.0 ml (0.25% w/v) of Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) were found to give maximum colour intensity. Hence, 2.0 ml each of Sulfanilamide (SAA), sulfadoxine (SDX) and sulfamethoxazole (SMX) were found appropriate.

The data depicted in (Table 1) 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. Excipients such as glucose, lactose, dextrose, starch, sodium alginate and sodium lauyrl sulphate did not interfere in the determination, while vitamin C was found to interfere (Table 2). The presence of glucose, lactose, dextrose, starch, sodium alginate, and sodium lauryl sulfate doesn't affect the accuracy of the determination. However, the presence of vitamin C does interfere and should be taken into consideration or addressed in some way. This could mean adjusting the procedure or taking steps to remove or account for the interference caused by vitamin C.

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

Material	Amount (mg)	% Recovery of cardanol* ± RSD**
Gluocose	50	97.5 ± 0.99
Lactose	50	99.3 ± 0.67
Dextrose	50	99.6 ± 0.45
Starch	50	100.3 ± 0.60
Sodium alginate	50	98.7 ± 0.97
Sodium lauryl sulphate	50	99.5 ± 0.64
Vitamin C	10	>50 < 60©

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

CONCLUSION

The procedures described in this paper are the first-ever use of sulfa drugs containing amino group as spectrophotometric reagents for the determination of cardanol, a phenolic compound found in agriculture by-product cashew nut shell liquid. Two important dimensions of this study include the success in finding new spectrophotometric reagents amongst the available myriad molecules in the field of pharmaceuticals which has a variety for the functional groups and molecular structure. Second, it will open up a new area of research on the dyes produced in the nation of cardanol with sulfa drugs potentially leading to the development of novel analytical techniques and applications in various fields.

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