Direct UV Spectrophotometric Estimation of β-Arteether

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A simple rapid, precise, accurate and highly specific spectrophotometric method has been developed for the determination of β-arteether in its pharmaceutical dosage forms. Arteether is a newer antimalarial derivative of artemisinin. Arteether has no UV absorption above 220 nm because of the absence of any chromophore group in its molecule. Therefore, it has to be degraded with 5M HCl, which produces chromophore groups that can absorb at 254 nm. Beer-Lambert law is followed in the concentration range of 5-50 μg/ml. The accuracy and reproducibility of the proposed method was statistically validated by variation studies.

β-Arteether is one of the artemisinin (Qinghaosu) derivatives, which has proved to be efficient against acute uncomplicated and severe falciparum malaria and can clear the parasite faster even in multiple drug resistant falciparum[1]. Literature survey revealed only methods based on electrochemical detection[2], TLC[3], densitometry[4], and spectrophotometric methods[5] (at wavelength 215 nm) for the estimation of β-arteether in samples and formulations. No direct spectrophotometric method is reported so far in literature for the drug estimation. The proposed method is simple and highly specific for determination of arteether in pharmaceutical dosage forms for routine estimation.

The UV spectrophotometer (Shimadzu 1601, Japan) with 1 cm matched quartz cells was used for absorbance measurements. All reagents used were of analytical grade. The stock solution of arteether (100 μg/ml) was prepared in methanol. Aliquots of standard solution representing 5-50 μg/ml of arteether were transferred into ten serially numbered test tubes and two millilitres of 5 M HCl was added to each. The solutions were kept in water bath at 50° for 30 min. for its acid decomposition to produceα, β- unsaturated decalone [8-methyl-5-(2-propanyl) decalin-4-ene3-one (fig. 1). Then these solutions were transferred to ten millilitre volumetric flasks and the volume was made upto 10 ml with methanol. The absorbance was measured at λ_{max} 254 nm using methanol as blank.

The problem of UV detection of arteether has been tackled by acid decomposition using 5 M HCl inducing the formation of UV detectable degradation product. The optimum conditions for the estimation of β-arteether were established by varying concentration of HCl and heating conditions. The maximum absorption was obtained by heating at 50° with 2 ml of 5 M HCl. Acid decomposition product give peaks at 254 nm, 310 nm, 357 nm; depending upon temperature, rate and time of heating and concentration of acid for decomposition. The peak at 254 nm is the most intense and prominent one and is produced in every condition of heating. It being much stable peak producing the most reproducible and linear range of absorbance, hence it was selected for the present study.

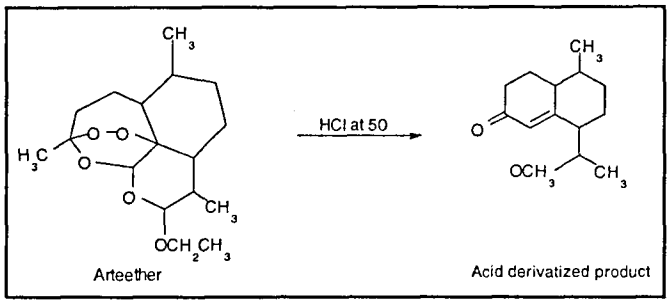

Fig. 1: Hydolysis and hydrolytic product of β-arteether

The calibration curve yielded coefficient of regression 0.9976 over Beer-Lambert range in 5-50 μg/ml. The regression equation was found to be: Absorbance=0.003302 (concentration)-0.0016. The molar absorptivity was found to be 9.31×10^3. The higher value of molar absorptivity indicated high sensitivity of the method. The lower values of standard

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deviation and coefficient of variation indicated the proposed method is accurate and highly precise.

Percentage variation was determined in known concentrations of drug sample prepared in methanol and after appropriate dilution using tripled distilled water to make up the concentration to 10, 20 and 30 μg/ml and independently developing absorbance by similar treatment thrice for each sample. Linearity of the procedure and effects on dilution of degraded species on absorbance were also determined. The absorbance for degraded 50 μg/ml equivalent of arteether samples and absorbance after dilution up to equivalent drug concentration up to 10, 20 and 30 μg/ml of degraded products were also determined using the standard curve so produced. The values of the concentration so determined and degree of variation from known concentrations were up to 96.5±0.32 % for direct determinations and for linearity of data upon dilution up to 98.5±0.56% shows that the results are highly reproducible and linear for the range even on dilution. The standard deviation of the readings for three studies in the range was also significant in the present method.

The procedure was used to determine the concentration of arteether in i.m. injection. Similar procedure was adopted by dilution of accurately measured volume with methanol to dilute and produce the desired theoretical concentration range up to 10 μg/ml, 20 μg/ml and 30 μg/ml. From the absorbance the approximate absorbance of arachis oil (used in i.m. injections) similarly diluted as previously determined by similar dilution was subtracted to determine the actual absorbance and extrapolated to determine corresponding amount of arteether. The concentration varied on an average 96±0.25% of original values, which shows that data are significant for determination of drug concentration in pharmaceuticals (Table 1). In conclusion, the proposed method is simple, rapid, accurate, specific and the reagents are cheaper that were used in the method. Further the procedure is direct involving simple methodology and not highly complicated and cumbersome as compared to other procedures for routine estimation of arteether in pharmaceuticals.

TABLE 1: VARIOUS EVALUATION CONSTANTS IN THE ESTIMATION OF ARTEETHER.

Parameters	Standards
λ_{max}	254 nm
Beer Law Limit	5-50 μg/ml
Sandell's Sensitivity (μg/cm²/0.001 A.U.)	1.28×10^{-3}
Molar Extinction Coefficient (Mole l cm⁻¹)	9.31×10^{8}
Correlation Coefficient	0.9976
Regression equations (mx+c) Slope (m)	0.003302
Intercept (c)	-0.0016
Adjusted R square	0.9948
Standard Error	3.6×10^{-3}

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