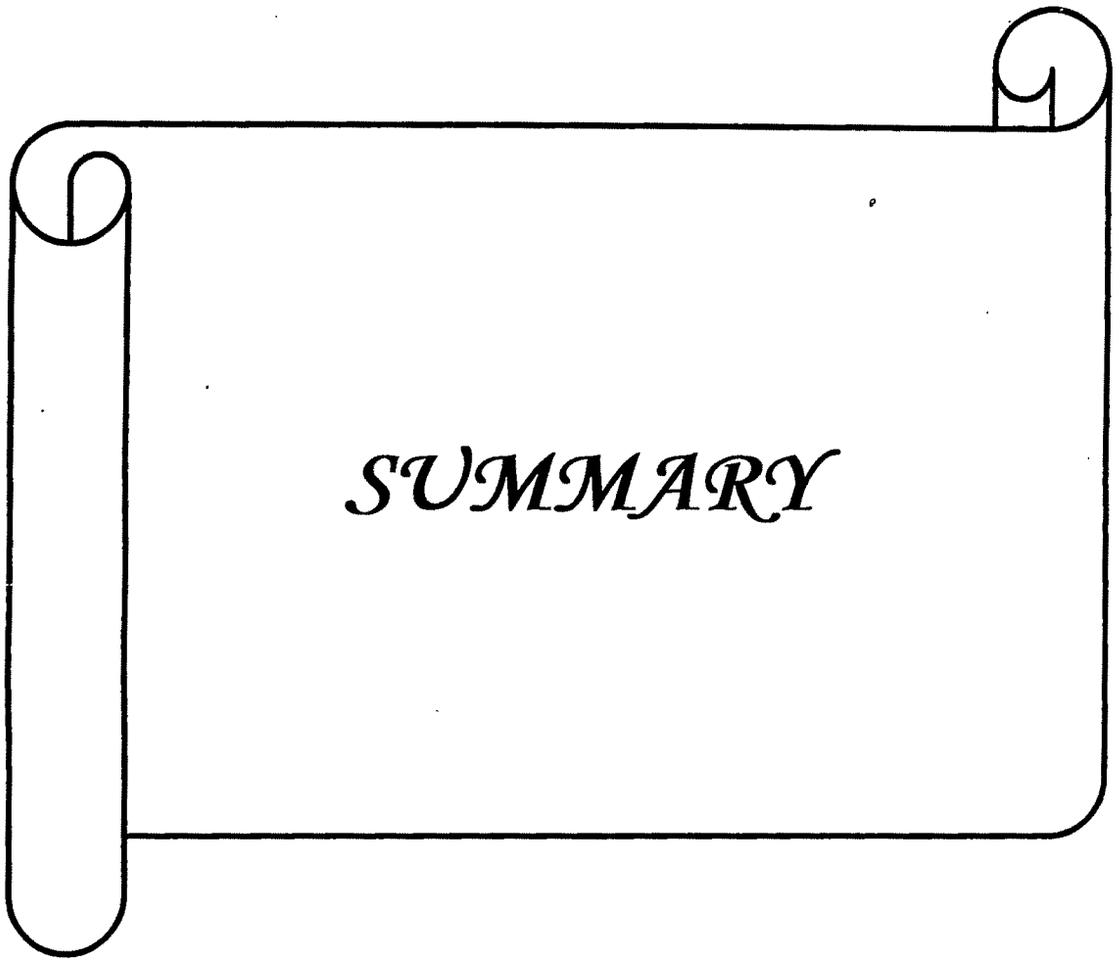
SUMMARY

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The thesis entitled ***"Microprocedure for the Determination of Some Organic and Medicinal Compounds"*** deals with the micro estimation of some simple and pharmaceutical organic compounds with Bromamine-B (sodium salt of N-bromo benzene sulphonamide) reagent in acidic medium.

The work incorporated in thesis has been divided into five chapters. The first chapter is introductory one. It describes about tupes of analysis, the scope of micro-analysis, the choice of the reagent, its preparation, standardisation, stability and reactive species.

The second chapter describes micro estimation of some phenols.viz. phenol, resocinol, pyrogallel, phloroglucinol, gallic acid, o-chlorophenol, m-chlorophenol, p-chlorophenol, O-nitrophenol, m-nitrophenol and p-nitrophenol with Bromamine-B reagent in acidic medium.

The third chapter describes micro estimation of some hydrazine derivatives viz. hydrazine sulphate, hydrazine dihydrochloride, phenyl hydrazine hydrochloride, 2,4-dinitro-phjenylhydrazien, semicarbazide and phenyl semicarbazide with Bromamine-B reagent in acidic medium.

The fourth chapter describes micro estimation of some acridine derivatives viz. acriflavine, proflavine, acridine orange and acridine yellow, with Bromamine-B reagent in acidic medium.

The fifth and last chapter describes micro estimation of some anti-hypertensive drugs viz. methyl dopa,propranolol and metoprolol with bromamine-Breagent in acidic medium. The method is also employed for determination of these compounds in their pharmaceutical preparations (Tablets) viz. Aldomet (Merind), Depamet (Stangen) Semrrina-250 (Boehringen-knoll), Inderal (Indian explosive), Ciplar (Cipla), Corbets (Sarabhai), Metoprolol (Cipla), Metocard (Torrent) and Lopressor Tablets (Hindustan Ciba-Geigy).

Bromamine-B ($C_6H_5SO_2NBrNa$), sodium salt of N-bromo Benzene sulphonamide, (BAB), is prepared by partial debromination of dibromamine-B which in turn prepared by the brominetion of chloramine-B Approximately 0.1N stock solution of BAB is prepared by dissolving 4gm of recrystalised compound in 250 ml distilled water and standardised iodometrically. Stock solution of BAB is fairly stable, its titre value does not change for several days when kept in Amber coloured bottle.

Bromamine-B a newly introduced oxidant acts as oxidising as well as brominating agent in both acidic and alkaline medium. Following equilibria are possible for BAB in acidic solution

$$C_6H_5SO_2N.NaBr \rightleftharpoons C_6H_5SO_2NBr^- + Na^+ \quad - \quad (1)$$

$$C_6H_5SO_2N\,Br^- + H_3^+O \rightleftharpoons C_6H_5SO_2NHBr + H_2O \quad - \quad (2)$$

$$2C_6H_5SO_2NHBr \rightleftharpoons C_6H_5SO_2NBr_2 + C_6H_5SO_2NH_2 - \quad (3)$$

$$C_6H_5SO_2NHBr + H_2O \rightleftharpoons C_6H_5SO_2NH_2 + HOBr \quad - \quad (4)$$

$$C_6H_5SO_2NBr_2 + H_2O \rightleftharpoons C_6H_5SO_2NHBr + HOBr \quad - \quad (5)$$

$$HOBr + H_2O \rightleftharpoons OBr^- + H_3^+O \quad - \quad (6)$$

It appears from above equilibria that aqueous solution of BAB gives several oxidising as well as brominating species. The stabilitiy of each species depends on the nature and pH of the medium. On the basis of several studies it has been suggested that depending upon the pH of the medium $C_6H_5SO_2NHBr$ or $C_6H_5SO_2NBr^-$ or $C_6H_5SO_2NBr_2$ are more likely oxidising species of BAB-While $C_6H_5SO_2NH_2Br^+$ and $C_6H_5SO_2NHBr$ are more likely brominating species in ac idic and slightly alkaline solution of BAB respectively.

It is obvious that Bromamine-B has potentialities of being adopted as an analytical reagent for a variety of simple and medicinal organic compounds. I have employed this reagent in

present thesis work for the micro estimation of phenols, hydrazine derivatives, acridines, and anti-hypertensive drugs in pure form as well as in their pharmaceutical preparations. The main object of the work is to give an entirely new method for the estimation of these compounds with the present reagent.

To establish reaction between reagent and redants (organic and pharmaceutical compounds), it is essential to know the molar ratio of BAB with reductants. Thus stoichiometry of reaction of BAB with every reductant is determined first.Furthe rin order to develop a suitable reaction condition effect of different variables such as effect of reaction time, concentration of sulphuric acid, concentration of bromamine-B reagent and reaction temperature are studied by selecting a test sample from every class of compounds (taken in present thesis work) viz. phenol from phenolic compounds, hydrazine sulphate from hydrazine derivatives, acriflavine from acrdines, and methyl dopa from anti-hypertensive drugs, On the basis of results obtained after studyhing the effect of different variables, a general procedure is recommended. With the recommended procedure micro estimation of some organic and pharmaceutical compounds are carried out.

For recovery of the sample back titration technique is adopted. The general procedure is as follows-

Aliquots 1_5 mg of the sample solution was taken in a 100ml Erlenmmeyer flask and 5mL of Bromamine-B (0.1N) solution was added, followed by 2mL of 2N-H_2SO_4.The flask was stoppered and contents were shaken thoroughly. The reaction mixture was allowed to stand at room temperature for prescribed reaction time (15-30 minuts). After the completion of reaction, the stopper was washed with 5mL of distilled water and 5mL of KI solution 10% was added to it. Contents were shaken thoroughly and kept for one minute, the liberated iodine was titrated with standard sodium thiosulphate solution (0.05N), using starch indicator, A blank experiment was also run under identical condition using all the reagent except the sample. The amount of the sample was calculated with the different in the titre value of the sample and blank by the following expression-

$$\text{mg of the sample} = \frac{MXNx(B-S)}{2Xn}$$

where,

M= molecular weight of the sample

N= normality of the sodium thiosulphate solution

B= Volume of the sodium thiosulphate solution with blank

S= Volume of the sodium thiosulphate solution with sample

n= stoichiometry of the reaction of BAB with Sample.

To find out validity and reproducibility of the recommended method percentage error, standard deviation and coeffecient of variation are calculated for every sample and sample size (1-5 mg).

In case of anti-hypertensive drugs to justify the validity of recommended method percentage recovery experiment was also carried out by standard drug addition method. Percentage recovery was calculated with the help of following expression.-

$$\%\ recovery = \frac{N\Sigma XY - \Sigma X(\Sigma Y)}{N(\Sigma X^2) - (\Sigma X)^2} \times 100$$

Where

X= amount of standard drung added

Y= amount obtained by recommended method

N(ΣN) = Number of observation

$\Sigma X^2 = \Sigma (NX)(X)$; $\Sigma X = \Sigma(NX)$

$\Sigma XY = \Sigma (NY)(X)$; $\Sigma Y = \Sigma(NY)$

The reagent and sample used are of analytical grade (Analar, BDH) or purified by recrystallisation.

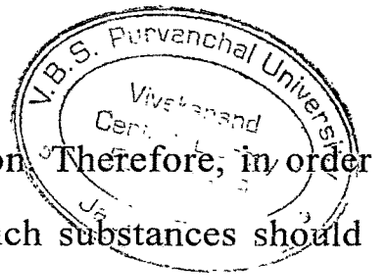
As described earlier the stoichiometry of reaction of sample with BAB is determined first. it is found that stoichiomedtry determined at prescribed reaction time is constant and reproducible. While studying the effect of reaction time on the recovery of sample it is noted that prescribed reaction time is essential for accurate and consistent results. The recovery of the sample within the prescribed reaction time becomes constant and increase of reaction time is meaningless. However, if a hasty experiment is done to save reaction time the percentage error is deplorable. The reason for higher values of negative error is due to incomplete reaction. The use of Bromamine-B reagent in a proper ionising medium has been studied. For this purpose glacial acetic acid, hydrochloric acid and sulphuric acid are tried as ionising medium. In these experiments an improvement in the reactivity of the reagent are noted. The use of sulphuric acid as ionising medium have got considerable effect. Thus, in the present work I have used the sulphuric acid as reaction medium. it is found that in present experiments 2mL of 2N-H_2SO_4 is sufficient to give accurate results. Bromamine-B reagent is the main reactive process. its concentration and the volume has got an important effect. Thus

the concentration of Bromamine-B reagent is varied and recovery of the sample is calculated. It is observed that o.1N concentration of the reagent (5mL) giveds quantitative and reprodu cible results and works well up to 5.0 mg of sample. While studying the effect of reaction temperature on the recovery of the sample, it is observed that the reagent is thermo-unstable. A temperature more than 30°C decomposes the reagent. Moreoever, if the reaction is carried out in ince-bath the reaction is very slow. Thus the suitable reaction temperature is room temperature (25-30°C).

The results obtained with the recommended method are described in second and subsequent chapters show that the percentage error are within $\pm$0.5-1.0%, the values of standard deviation (SD) and the coefficient of variations are less than 1.0%. The percentage recovery of anti-hypertensive drugs are lying within 99-0-100.1%.

Further based on the stoichiometry of reaction of sample with Bromamine-B reagent, literature available, isolation and identification of reaction products, the possible course of reaction of every sample with the reagent has been discussed.

The effect of interfering susbstances are also studied.It is found that the presence of easily oxidisable substancves such as phenols, amines, aromatic amines, amino acids, thioureas and



hydroxy acids interfere in determination. Therefore, in order to get accurate results the presence of such substances should be avoided. However, the expipients of tablets such as talcum powder, magnesium powder and $CaCO_3$ et. do not interfere in determination.