```
30 IF A >= 4 THEN 60 ELSE 40

40 KR1 = KR1 - 0.01

50 GOTO 20

60 PRINT KR1

70 END
```

Thus from **fig 2.** one can calculate the loading dose, the total duration over which the formulation is to spurt the drug in the body, and the time at which release of maintenance begins. **Fig. 3** will help the formulation designer to calculate release kinetic profile and maintenance dose.

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# Extractive Spectrophotometric Determination of Antihistaminic Drugs


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**A sensitive spectrophotometric method has been developed for determining orphenadrine and diphenyldramine hydrochlorides from its pharmaceutical formulation based on solvent extraction into chloroform of the complexes formed with bromocresol green, bromophenol blue and methyl orange. Complex formation and extraction was complete and quantitative at pH 4. Direct determinations in capsule and tablet preparations were carried out satisfactorily and the average recovery was 100±1.0%.**


ORPHENADRINE hydrochloride (ORH) and diphenhydramine hydrochloride (DPH) are antihistaminic agents. Orphenadrine hydrochloride is frequently used in the therapy of parkinsons disease and drug-induced parkinsonism. It has been in use for many years and studies of its metabolic fate in the rat, monkey and man have reported.[1] Spectrophotometric.[2,3] and chromatographic[4,5] methods have been proposed for the determination of ORH. However, these methods are complicated and not sensitive enough. Diphenhydramine, an antihistamine drug that is used in various formulations is analysed by method such as nonaqueous titration[6], potentiometric titration[7], ion-exchange separation[8], quantitative thin layer chromatography,[9] fluorimetric[10] and other routine techniques. However these methods lack the simplicity and sensitivity for routine analysis of pharmaceutical preparations. Spectrphotometric methods have also been used for the analysis of the base. Ion-pair formation with

**Table 1: Optical characteristics of drg dye complexes in chloroform (For each reagent 2 ml of buffer pH 4 was used)**

| Compounds | Name of reagent | Amount of reagent ml | λmax nm | Beer's law range (μg/ml) | C x $10^3$ 1/mol/cm | Sandell's sensitivity (μg/$cm^2$) | RSD |
|---|---|---|---|---|---|---|---|
| ORH | BCG | 2 | 440 | 1-25 | 7.3 | 0.0421 | 1.4 |
| | BPB | 1.5 | 430 | 0.5-20 | 6.1 | 0.055 | 1.0 |
| | MO | 1 | 430 | 2-25 | 5.5 | 0.0507 | 1.4 |
| DPH | BCG | 1 | 430 | 1-15 | 9.1 | 0.0321 | 1.2 |
| | BPB | 1 | 430 | 1-15 | 9.1 | 0.0321 | 1.0 |
| | MO | 2.5 | 440 | 1.20 | 7.0 | 0.0422 | 1.6 |

**Table 2: Analysis of drug in pahrmaceutical products**

| Sample Tab/Caps | Claim mg | Recovery % Official method | proposed method* A | B | C |
|---|---|---|---|---|---|
| ORH | | | | | |
| Orphipal | 50 | 98.9 | 100.1 | 100.3 | 99.9 |
| DPP | | | | | |
| Benadryl | 25 | 99.8 | 99.9 | 100.1 | 99.7 |

*Average for five determinations. A=BCG, B=BB,C =MO.

tetrabromo flourescein[11] complex formation with zincon and cupric chloride[12], interaction with cobaltous thiocyanate[13] and precipitation with ammonium reineckate,[14] molybdophosphoric acid[15] were the bases of some of the reported spectrophotometric methods.

A JASCO model UVIDEC-610 UV-VIS spectrophotometer with 1.0 cm matched cells was used for absorbance measurements. All the analytical grade materials were used. Solutions of bromocresol green (BCG), bromophenol blue (BPB) and methyl orange (MO) were prepared in double distilled water (0.1% w/v). Potassium hydrogen phthalate buffer solution of pH 4 was prepared in distilled water. A working standard solution of ORH and DPH of concentrations equal to 100 μg was prepared by dissolving requisite amounts of pure drugs in double distilled water.

A suitable aliquot of ORH or DPH solution was pipetted into a series of separating funnels. To each funnel, buffer and dye solutions were added as mentioned in **Table 1**. Ten ml of chloroform was added to each funnel. The contents were shaken vigorously and left at room temperature for two minutes. The two phases were allowed to separate and the chloroform layer passed through anhydrous sodium sulphate. Absorbance values of the chloroform layers were measured against their respective reagent

blank at the wavelength of maximum absorbance (Table 1).

Powdered tablets or the contents of a capsule equivalent to 100 μg of ORH DPH were dissolved in distilled water. The solutions were filtered and the combined filtrate were collected in a 100 ml standard flask and diluted with distilled water. Suitable volume of the aliquots of each solution was analysed by the general procedure.

The yellow colour of the ion-pair complexes formed are very stable over a period of 10 h at room temperature. The yellow color of ion-associated complexes can be easily measured at 430- 440 nm against reagent blank. The proposed method is simple, fast and accurate. It does not suffer any interference due to common excipients like talc, starch, stearic acid, sodium alginate and gelatin. The low values of relative standard indicate that high accuracy of the method. All results of analyses are presented in a Table 1 and Table 2 and are in good agreement with those of official methods.[16,17] Hence, the proposed methods are simple, reproducible and can conveniently be used for routine analytical work.

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