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DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR DOMPERIDONE CONTAINING PIPERIDINE IMPURITY

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Abstract:- Domperidone IUPAC name 5-chloro- l-(l-[3-(2-oxo-2,3-dihydro-l//-benzo[JJimidazol-1 -yl)propyl]piperidin-4-yl)-l//-benzo[f/]imidazol-2(3//)-one

Keywords: development And Validation

INTRODUCTION :-

It is a peripheral dopamine (D2) and (D3) receptor antagonist. It provides relief from nausea by blocking receptors at the chemo-receptor trigger zone (a location in the nervous system that registers nausea).

There are different methods are reported for determination of assay, presevatives and impurities in domperidone drug but in present work we first time used derivatisation procedure followed by RP-HPLC method for detection of piperidine impurity in Domperidone.

Experimental

Method parameters and Procedure Chromatographic conditions

Instrument: The Agilent chromatographic system with UV detectionsystem.
Column: Agilent zorbax Cl8 column (250 x 4.60 x5(j,m)
Mobile phase A: 2.72 gm of KH2PO4 in 1000ml of water.
Mobile phase B: Acetonitrile Gradient elution of mobile phase
Flow rate: lml/min
Temp : column oven and sample compartment : 25°C Wavelength: 235nm Injection volume :10µ1
Diluent: Methanol

Gradient Programme:

Time (min)	Mobile phase A (%)	Mobile phase B (%)
0	90	10
5	90	10
50	70	30
55	50	50
60	90	10
65	90	10

Solution Preparation:
Standard stock solution : 10 mg of piperidine -4-Carboxylic acid dissolved in methanol and diluted in 100 ml volumetric flask.
Test solution: 10mg sample diluted with methanol in to 50ml volumetric flask.
Standard solution : 2.0 ml of standard stock solution taken in 100 ml volumetric flask and diluted to volume with diluent. Transferred 5.0 ml of this solution in 50 ml test tube.
Test solution : Weighed and transferred 10.o mg of sample in 50 ml test tube added 5 ml of diluent and sonicated to dissolve.
Derivatisation solution
Weighed about 100 mg of benzyl chloride transferred in to a 100 ml amber coloured volumetric flask then dissolved and diluted with acetonitrile.
Derivatisation Buffer
0.1 M solution of disodium hydrogen phosphate dehydrated in water.

Derivatisation buffer

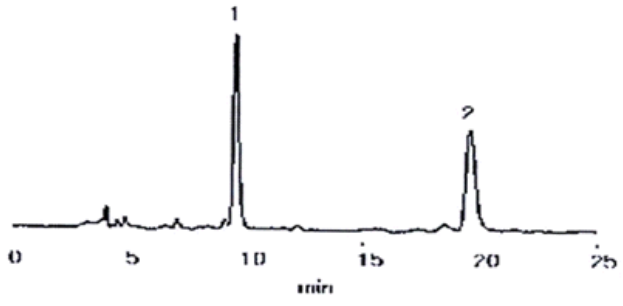
Added 5.0 ml of derivatisation buffer in each of three 50 ml test tubes containing 5ml of blank (diluent), 5 ml of Standard solution and 5ml of test solution mixed on cyclomixer for 10 seconds and adjusted pH to 8.0 with very dilute orthophospheric acid solution. Then added 5.0 ml of derivatisation solution and mixed on cyclomixer for 40-50 seconds.Then transferred the respective solution in to separate 25ml volumetric flask. Rinsed the test tube with two three quantities of about 3ml of derivatisation buffer and transferred the rinse to the same and diluted to volume with derivatisation buffer.

Procedure

Injected derivated blank .standard solution in six replicates and then Test solution. Recorded the chromatogram and measured the peak responses .Relative standard deviation observed for peak area of Piperidine -4-carboxylic acid in standard solution was not more than 5.0%.
Calculation of Piperidine 4-carboxvlic acid content
Content Piperidine -4-carboxylic acid (in ppm)
= AT/As x Ws/100 x 2/100 x 5/WT x 106 Where
At- Area of piperidine-4-carboxylic acid in test solution.
As -Mean area of piperidine-4-carboxylic acid in standard solution.
Ws- Weight of piperidine-4-carboxylic acid in standard solution in mg.
WT- Weight of sample in mg.

Chromatogram

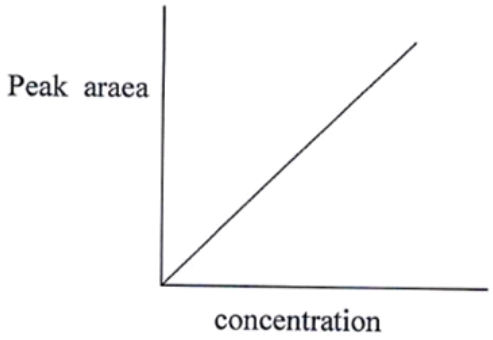
The below chromatogram showimg peak for impurity and standard respectively.



Validation

The method validation carried out on following parameters

Linearity: Calibration curve plotted between concentration in ppm against peak response. The curve obtained is linear passing through origin.



Specificity: Peak purities higher than 99.3% were obtained for the chromatograms of samplesolutions, demonstrating that other compounds did notco-elute with the main peaks.

Robustness:

Statistical analysis showed no significant difference betweenresults obtained employing the analytical conditions establishedfor the method and those obtained in the experiments in which variations of some parameters were introduced. Thus, the method showed to be robust for changes in mobile phaseflow rate 1.0 and 1.3ml/min, buffer proportion (±2% of organic solvent), mobile phase pH 7.5 to 8.0

Limit of detection (LOD) and limit of quantification (LOQ)

The LOD and LOQ of impuritie were estimated based on the signal-to-noise ratio to get a signal-to-noise ratio of 3:1 and 10:1, respectively, for each impurity by injecting a series of dilute solutions with known concentration. Precision and accuracy studies were also carried out at the LOQ level by injecting six individual preparations of impurities and calculating the % RSD of the area

Result and conclusions

A statistical comparison of the results obtained by the proposed methods and those obtained by the other method shows good correlation. The proposed RP-HPLC methods give comparable results and did not suffer from any interferences by many pharmaceutical additives, diluents and activeingredients commonly used in drug formulations. The method has the advantages of higha ccuracy.
The result obtained and statistical analysis proves that the method is significant and sensitive for the determination of piperidine impurity in domperidone.

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