Spectrophotometric Methods Development and Validation of Budesonide in Bulk and Marketed Formulation

V.S. Madankar*, S.D. Jadhav, N.B. Londhe.

Abstract:

The present work reveled that UV Spectrophotometric method was developed for the quantitative determination of Budesonide in bulk drug and pharmaceutical dosage forms and has an absorption maximum at 240 nm in distilled water. The Beer's law was obeyed over the concentration range of 10-80 µg/ml. The correlation coefficient was found to be 0.999 and it has showed good linearity, reproducibility, precision in this concentration range. The % recovery values were found to be within 99.23%showed that the method was accurate. The LOD and LOQ were found to be 0.461073 µg /ml and 1.39719µg/ml respectively.

Keywords: Spectrophotometric Methods, IR, UV, Validation, Budesonide.

Introduction:

Ultraviolet-Visible Spectro-photometry is one of the most frequently employed techniques in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region are called Ultraviolet-Visible spectrophotometers. Infrared Spectroscopy is one of the most powerful analytical techniques which offer the possibility of chemical identification. Budesonide (BUD) is a water insoluble nonsteroidal glucocorticoid used for the maintain therapy to asthma[8, 9] Till today, the application of SLNs in BUD delivery has not been reported yet. In the present study, we prepared Bud SLNs, completed the optimization of the formula, and characterized the properties and structure of the Bud SLNs. pulmonary route presents several advantages in treatment of respiratory diseases. Drug inhalation enables a rapid and predictable onset of action and induces fewer side effects than administration by other routes[1].

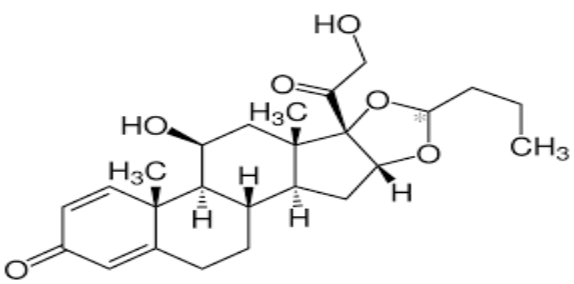

Fig: Molecular Structure of Budesonide.

(16, 17-(butylidene bis (oxy))-11, 21-dihydroxy-, (11-β, 16-α)-pregna-1, 4-diene-3, 20-Dione.

Material and Methods

Materials:

Drugs:

Budesonide Micronized (BUD) was obtained from Murali Krishna (Ranjangaon, India),

Budesonide dry powder inhalation commercial product was purchased from local market.

Chemicals:

Methanol, Potassium Bromide (Shivaji Scientific Supplier, Pune)

*Instruments used***:**

Jasco 1800 spectrophotometers with 1 cm matched quartz cell were used.[3]

IR Techniques:

This technique when coupled with intensity measurements may be used for quantitative analysis and methods of structural analysis (X-Ray diffraction, electron spin resonance, etc) is that it provides useful information about the structure of molecule quickly, without tiresome evaluation method. Thus, an IR spectrum of a chemical substance is a fingerprint for its identification.

Preparation of reagents:

Weighed accurately 0.1 g of Budesonide and transferred in to 100 ml of volumetric flask already containing 20ml methanol and volume was made up to the mark with distilled water (1000 µg /ml). Further dilution of 100 µg /ml solution of Budesonide was made using Distilled Water.

Preparation of standard stock solution

Stock solution of Budesonide 100 µg /ml was prepared in distilled water .From this stock solution, appropriate dilution was made and scanned in the UV range 200-400 nm. The absorbance of Budesonide was found to be 240 nm. This increased solubility of Budesonide is due to the hydrotropic solubilization phenomenon. Aliquots of in the range of 10-80µg /ml were prepared with the same solvent and scanned under Photometric mode for Absorbance at 240 nm[9].

Experimental:

*Preparation of standard calibration curve of bulk drug***.**

1. Preparation of standard stock solution

Accurately weighed and transferred 0.1 gm. Budesonide (bulk drug) in 100 ml volumetric flask and dissolved in 20 ml methanol & diluted with distilled water (1000 µg/ml Stock solution A). From the stock solution, 10 ml was withdrawal and transferred in to 100ml volumetric flask containing distilled water. Further dilutions were made to obtain the final concentration of 100 µg/ml.

2. Preparation of calibration curve

Fresh aliquots of Budesonide from 1.0-8.0ml (10µg/ ml-80µg/ml) were transferred into a series of 10 ml volumetric flasks to provide final concentration range of 10-80µg/ml. The solutions in each flask were made up to the mark with distilled water. The absorbance of solution was measured at 240 nm against the reagent blank. The amount of Budesonide in the sample solution was computed from its calibration curve.

3. Results and Discussion

UV method validation of drug:-

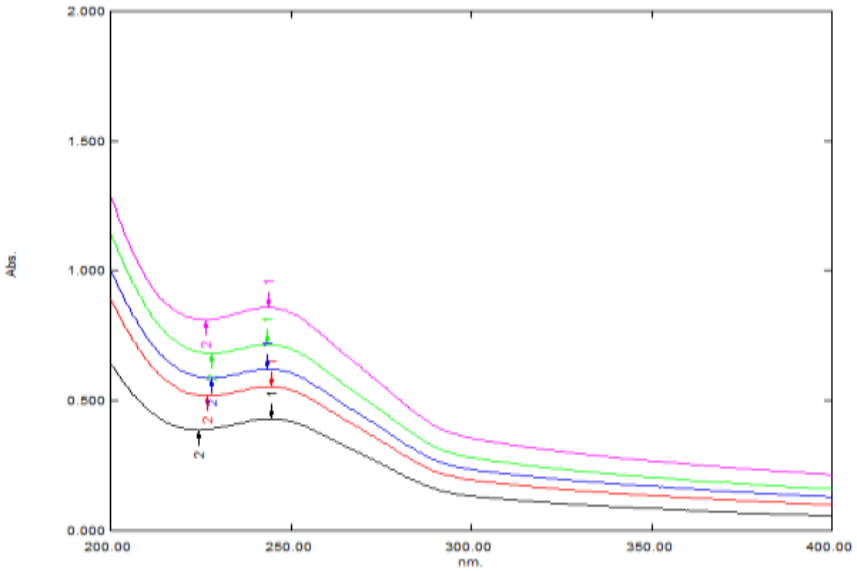

Fig 2: Overlain Spectra of Budesonide.

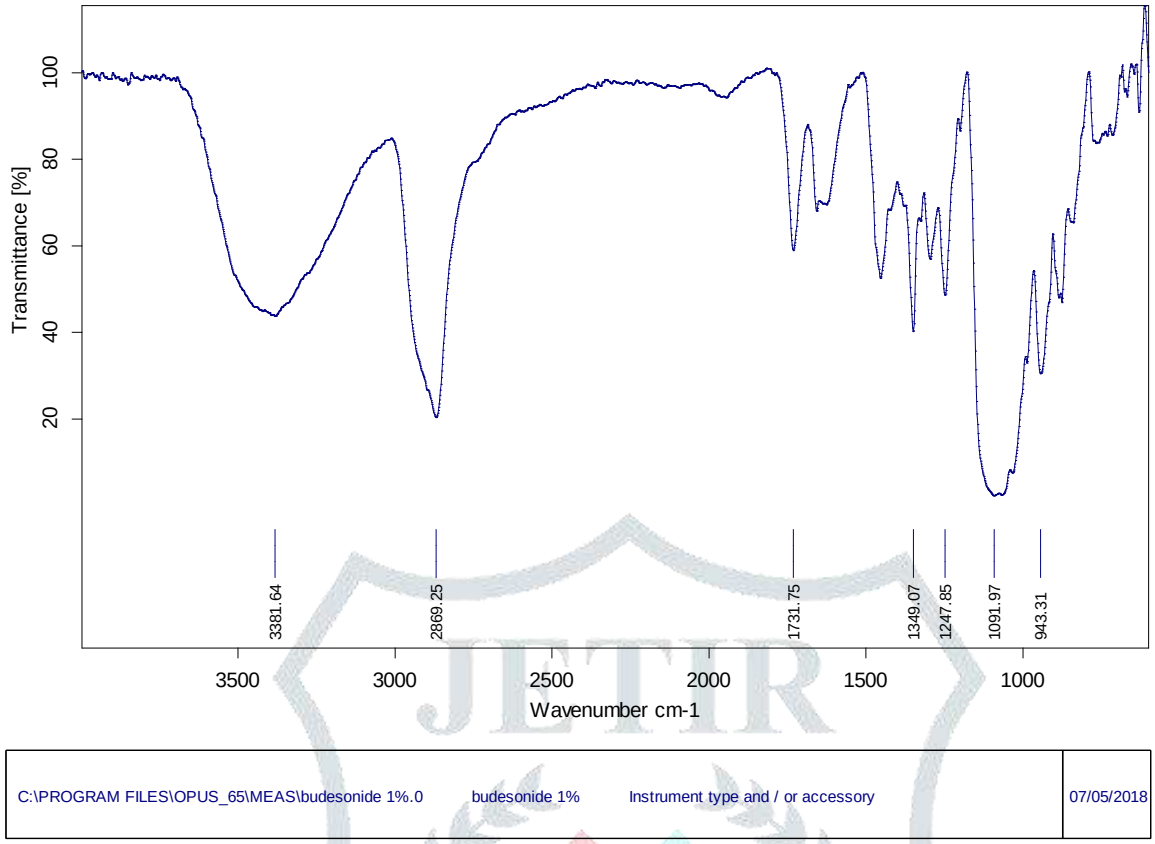

Fig 3: IR spectra of Budesonide.

Table 1: Interpretation of Budesonide.

Sr. No.	Functional Group	Frequency (cm^{-1})
1	-OH (Hydroxyl)	3081.64
2	-CH (Aldehyde)	2869.25
3	-C=O (Aldehyde)	1731.75
4	-C=C (Aromatic)	1475
5	-C-C (Aromatic)	1349.07
6	-C-O (Alcohols)	1247.85

The UV method was developed for synthesized impurity as per ICH (Q2B) guidelines.[4]

Linearity: The synthesized impurity shows maximum absorbance at 240 nm and obeys Beer-Lamberts law in the concentration range of 10-80µg/ml.

Table 2: Linearity of Budesonide

Sr .No.	Conc. (µg/ml.)	Absorbance at 240nm
1.	10	0.267
2.	20	0.349
3.	30	0.503

4.	40	0.692
5.	50	0.788
6.	60	0.992
7.	70	1.12
8.	80	1.23

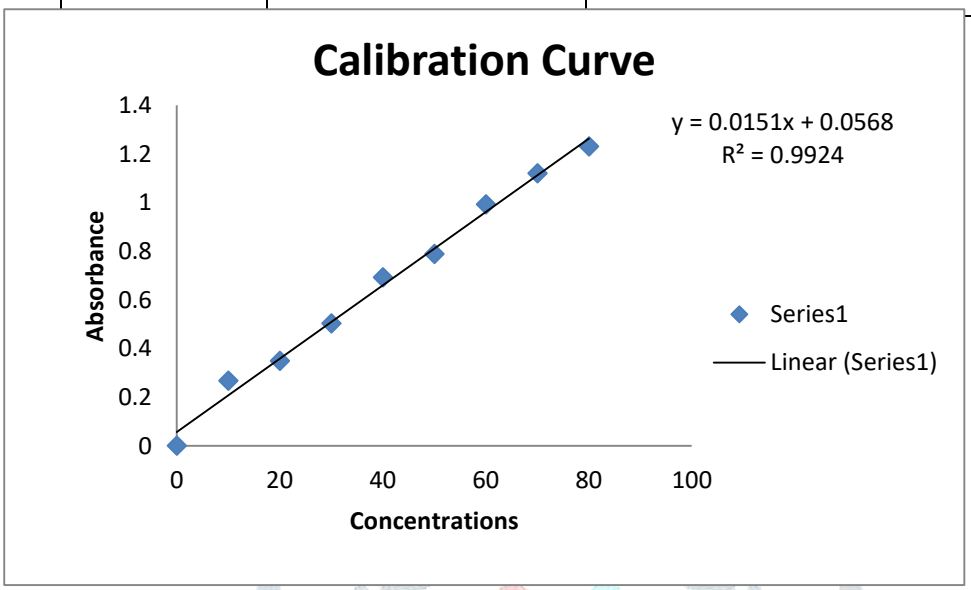

Fig 3: Calibration Curve of Budesonide.

Precision: Precision of the method was demonstrated by intra-day and inter-day variation studies. The precision of an analytical method is the degree of agreement among individuals.

Table 3: Precision (Interday & Intraday study) of Budesonide

Conc.	**Abs(0min)**	**Abs(1 day)**	**Abs(2d)ay**
40	0.599	0.591	0.598
40	0.601	0.598	0.573
40	0.616	0.614	0.598
40	0.595	0.584	0.588
40	0.593	0.596	0.575
40	0.601	0.588	0.581
Average	0.600833	0.595167	0.5855
SD	0.00811	0.010553	0.011005
RSD%	1.349736	1.773124	1.879512

Test results when the method is applied repeatedly to multiple samplings of homogenous samples. It provides an indication of random error results and was expressed as coefficient of variation (CV).

Robustness: Study by change in solvent.

Table 4: Robustness of Budesonide

Conc. (µg/ml)	**Abs** (240nm)	**Abs** (259nm)
40	0.598	0.578
40	0.597	0.575
40	0.6	0.577
40	0.607	0.595
40	0.598	0.571
40	0.588	0.577
Average	0.598	0.578833
SD	0.006099	0.008305
RSD	1.01993	1.434716

Ruggedness: Study of change in solvents.

Table 5: Ruggedness of Budesonide.

Conc. (µg/ml)	**Abs (Methanol)**	**Abs (ACN)**
40	0.598	0.595
40	0.591	0.598
40	0.6	0.612
40	0.617	0.581
40	0.598	0.589
40	0.593	0.586
Average	0.5995	0.5935
SD	0.009225	0.010932
RSD%	1.538777	1.841888

Accuracy: Accuracy is the closeness of the test results obtained by the method to the true value. To study the accuracy, 20 tablets of each brand were weighed and powdered. Various Dilutions of sample solution were prepared. Analysis of the same was carried out. Recovery studies were carried

out at three different levels i.e.50%, 100% and 150% *b*y adding standard drug solution to the sample solution.

Table 6: Accuracy of Budesonide.

Tablets	Amount of sample (µg/ml.)	Amount of drug (µg/ml.)	% recovery
50	10	5	99.03
100	10	10	99.16
150	10	15	99.51

Conclusions

The proposed method for the estimation of Budesonide was found to be simple, sensitive and reliable with good precision and accuracy. The developed Spectrophotometric method was validated for estimation of Budesonide using accuracy, precision, linearity, range and robustness, %R.S.D for all parameter were found to be less than 2, and it indicates the validity of method. Assay results showed the accuracy of proposed method for estimation of Budesonide. This method can be conveniently employed for the routine analysis and the quality control of Budesonide in pharmaceutical dosage forms. The sample recovery from the formulation was in good agreement with its respective label claim.

Acknowledgments

The authors thankful to Prof. T .J. Sawant, JSPM, Pune for his kind co-operation and also thankful to Dr. S. B. Wankhede , Principal, JSPM's Charak College of Pharmacy & Research for providing necessary facilities to carry out the research work.

References

1. Naikwade S., Bajaj A., Preparation and In Vitro Evaluation of Budesonide Spray Dried Micro particles for Pulmonary Delivery. C. U. Shah College of Pharmacy, S.N.D.T. Women's University, Juhu-Tara Road, Santacruz (W), Mumbai-400049, Maharashtra, India Sci Pharm. (2009), (77): 419–441.

2. Khilnani G, Banga A. Aerosol therapy. J Indian Acad Clin Med. (2004), (5): 114–123.

3. Newman S.P, Busse W.W. Evolution of dry powder inhaler design, formulation and performance. Respir Med. (2002), (96): 293–304.

4. Telko M.J, Hickey A.J. Dry powder inhaler formulation. Respir Care. (2005), (50): 1209–1227.

5. Szafranski W, Cukier A, Ramirez A, Mengaz G, Sansores R, Nahabedian S, Peterson S, Olsson H. Efficacy and safety of budesonide/formoterol in the management of chronic obstructive pulmonary disease. Eur Respir J. (2003), (21): 74–81.

6. Larhrib H, Martin G.P, Marriott C, Prime D. The influence of carrier and drug morphology on drug delivery from dry powder formulations. Int J Pharm. (2003), (257): 283–296.

7. Yu Z, Rogers T.L, Hu J, Johnston K.P, Williams R.O. Preparation and characterization of micro particles containing peptide produced by a novel process: spray freezing into liquid. Eur J Pharm Bio pharm. (2002), (54): 221–228.

8. Zhang P. R, Ying F. T, Wang S, Wang Y, Ying X, Miao L, Yi G, Preparation and characterization of budesonide loaded solid lipid nanoparticles for pulmonary delivery. Journal of Chinese Pharmaceutical Sciences. (2011), (04): 049.

9. Richard N. F, Lana B., Advanced Drug Delivery. Rev. (2005), (57): 303–316.

10. Umaretiya G.M, Patel P.R, Patel J. K Formulation and Characterization of Solid Lipid Nanoparticles Dry Powder Inhaler containing Triamcinolone Acetonide. International Journal of Research in Pharmacy and Chemistry. (2011), (3): 2231–2781.

11. Kumon M, Machida S, Suzuki M, Kusai A, Yonemochi E and Terada K. Application and Mechanism of inhalation profile Improvement of DPI Formulations by Mechanofusion with Magnesium Stearate. Chem Pharm Bull. (2008), 56(5):617–625.

12. Fults K, Miller I, Hickey A. Effect of Particle Morphology on Emitted Dose of Fatty Acid Treated Disodium Cromoglycate Powder Aerosols. Pharm Dev. Technol. (1997), 2(1): 67–79.

13. Shah S. P and Misra A. Development of Liposomal Amphotericin B Dry Powder Inhaler Formulation. Drug Delivery. (2004), 11(4): 247-53.

14. Lu D and Hickey A. Liposomal Dry Powders as Aerosols for Pulmonary Delivery of Proteins. AAPS Pharm SciTech. (2005), 6(4): 80. E641-E648.

15. Joshi M. R and Misra A. Liposomal Budesonide for Dry Powder Inhaler: Preparation and Stabilization. AAPS Pharm Sci Tech. (2001), 30(2): 25-31.

16. Ausborn M and Nuhn P. Possibilities and Problems Concerning the Stabilization of Liposomes by Freezing and Lyophilisation. PZ Wissenschaft, (1990), (135): 183-188.

17. Mali A.J, Pawar A.P, Purohit R.N. Development of Budesonide Loaded Biopolymer Based Dry Powder Inhaler: Optimization, *In Vitro* Deposition, and Cytotoxicity Study. Journal of Pharmaceutics (2014), (1): 1-12.

18. Farooq U, Malviya R and Sharma P, Et Al. Extraction and Characterization of Okra Mucilage as Pharmaceutical Excipient. Academic Journal of Plant Sciences, (2013), (6): 168-172.

19. Andrade F, Goycoolea F, Chiappetta D. A, Neves J, Sosnik A, and Sarmento B. Chitosan-grafed copolymers and chitosan-ligand conjugates as matrices for pulmonary drug delivery. International Journal of Carbohydrate Chemistry, (2011), (14): 2011.

20. Crcarevska M, Dodov M, and Goracinova K, Chitosan coated Ca-alginate micro particles loaded with budesonide for delivery to the inflamed colonic mucosa. European Journal of Pharmaceutics and Bio pharmaceutics, (2008), (68) (3): 565–578.

21. Patil A.T., Patil S.D., Shaikh K.A.; Sensitive LC method for simultaneous estimation of ciclesonide and Formoterol fumarate in dry powder inhaler. Journal of Liquid Chromatography & Related Technologies; (2011): 34(15).

22. Kale N.R, Dr. Pingle A.P, Mirza J. A, Dhongade G. N. Rp-Hplc Method for Simultaneous Estimation of Formoterol Fumarate and Budesonide in Metered Dose Inhaler Formulation. World Journal of Pharmaceutical Research, (2014), (3) (6): 1386.