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Research Article

# UV Spectrophotometric Method Development and Validation of Butorphanol Tartrate in Bulk Drug and Pharmaceutical Formulation

Sonu Ahirwar [1]*, Varsha Kashaw [2], Ravish Sahu [1], Surbhi Chourasia [3], Vaibhav Rajoria [3], Prakash Kushwaha [1]

[1] *Vedic College of Pharmacy, Rehli Rd, Bapupura, Sironja, Sagar (M.P), 470228*

[2] *Sagar Institute of Pharmaceutical Sciences (SIPS), Patheriya Jat, Sagar, MP, 470003*

[3] *Vedic Institute of Pharmaceutical Education and Research, University, Rehli Rd, Bapupura, Sironja, Sagar (M.P), 470228*

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*Address for Correspondence:

Sonu Ahirwar, Vedic College of Pharmacy, Rehli Rd, Bapupura, Sironja, Sagar (M.P), 470228

## Abstract

The present research work discusses the development and validation of a UV spectrophotometric method for butorphanol tartrate. Simple, accurate and cost efficient spectrophotometric method has been developed for the estimation of butorphanol tartrate in tablet dosage form. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λ max) was found to be 278nm. The percentage recovery of butorphanol tartrate was in the 100.016±0.68. Beers law was obeyed in the concentration range of 2-12µg/ml. Calibration curves shows a linear relationship between the absorbance and concentration. The line equation y = 0.0674x - 0.0057 with r2 of 0.9998was obtained. Validation was performed according to ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The sample solution was stable up to 36 hours. The proposed method may be suitable for the analysis of butorphanol tartrate in tablet formulation for quality control purposes.

**Keywords:** Butorphanol tartrate, Validation, Precision, Accuracy, LOQ, LOD, ICH guidelines.

## INTRODUCTION

An effective postoperative pain management regimen is vital to patient recovery after surgery. Multi-modal analgesia, using different classes of analgesics, is the currently recommended method to obtain this goal[1,2] . Of the multi-modal approach, adding an adjunct to an opioid-based intravenous (i.v.) patient-controlled analgesia (PCA) as a convenient regimen for moderately severe pain control is popularity used worldwide in clinical practice[3]. Various adjunct drugs, such as nonsteroidal anti-inflammatory drugs[4,5], N-methyl-D-aspartate (NMDA) antagonists[6], antiemetic[7], alpha-2 adrenergic agonists[8], and glucocorticoids[9] have been used in these multi-modal protocols. Butorphanol tartrate (Figure 1) is a mixed agonist–antagonist opioid with strong κ-receptor agonist and weak μ-receptor antagonist activity. Chemically, it is morphinan-3,14-diol,17-(cyclobutylmethyl)-, (–)-, [S-(R*,R*)]-2,3-dihydroxy butanedioate (1:1) (salt). Butorphanol tartrate is commonly used for the management of cancer, postoperative, gynecologic, and obstetric pain. As with other opioid analgesics, patient-controlled analgesia (PCA) butorphanol tartrate is associated with troublesome side effects such as nausea and/or vomiting, somnolence, and dizziness[10,11]. To the best of our knowledge, few data are available about compatibility and stability of butorphanol in combination with other drugs[12-16]. Most of these methods are uneconomic and involving complex sample preparation. So, there is a need for the development of simple sensitive effective and economic methods and hence the present work was planned to validate the UV spectroscopic method for butorphanol tartrate in tablet formulations by using following parameter like accuracy, precision, linearity and range, limit of detection, limit of quantification, specificity, robustness, ruggedness and system suitability as per ICH guidelines[17,18]. The aim of present work is to find out a simple, sensitive, specific, spectrophotometric method for the detection of butorphanol tartrate in pharmaceutical tablet formulation.

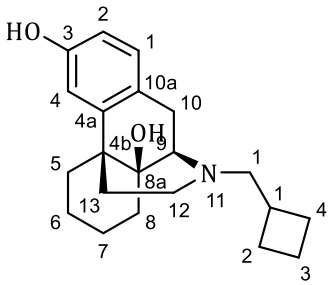


**Figure 1 Chemical structure of butorphanol tartrate**

## EXPERIMENTAL

### Reagents and chemicals

Butorphanol tartrate (Pure drug) was received as gift sample from Pfizer, India. All the other chemicals and solvents used were of analytical grade. Marketed formulation of butorphanol tartrate is *Torbutrol* 10 mg tablet (*Torbutrol* is a registered trademark of Zoetis, Canada) is purchased from GNH India. Triple distilled water was generated in house. All solvents and reagents were of analytical grade. All the solutions were protected for light and were analyzed on the day of preparations.

### Instrument

A double beam UV/Visible model 1800, Shimadzu, Japan, with software UV Probe 2.10 and 1 cm quartz cell, was used for analysis. For weighing, Wenser (max 200g, sensitive = 0.1 mg) balance was used.

### Determination of wavelength of maximum absorbance ($\lambda_{max}$) of butorphanol tartrate

Wavelength of maximum absorption was determined by scanning 10µg/ml solution of butorphanol tartrate using UV spectrophotometer from 200 to 400 nm. This showed maximum absorbance at 278 nm (Fig. 2).

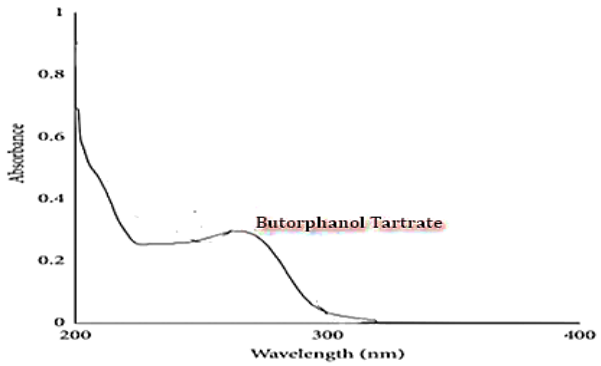


**Figure 2: Determination of λ max of butorphanol tartrate**

### Preparation of standard stock solution (Stock-A)

Standard stock solutions were prepared by dissolving 100 mg of drug in 100 ml of 0.05M sulfuric acid: distilled water (70:30; %v/v) and the flask was sonicated for about 10 min to solubilized the drug and the volume was made up to the mark with 0.05M sulfuric acid: distilled water (70:30; %v/v) to get a concentration of 1000 µg/ml (Stock-A) for drug.

### Preparation of working standard solution

From stock solutions of butorphanol tartrate 1 ml was taken and diluted up to 100 ml separate volumetric flask. From this solution 0.2 to1.2ml solutions were transferred to 100ml volumetric flasks and make up the volume up to 100 ml with 0.05M sulfuric acid: distilled water (70:30; %v/v), gives standard drug solution of 2-12µg/ml concentrations of butorphanol tartrate.

### Preparation of the calibration curves of the drug

The calibration curve was prepared by scanning test samples ranging from 2-12µg/ ml at 278nm for butorphanol tartrate. The calibration curve was tested by validating it with inter-day and intra-day measurements. Mean of n =5 determinations was plotted as the standard curve (Fig.3).

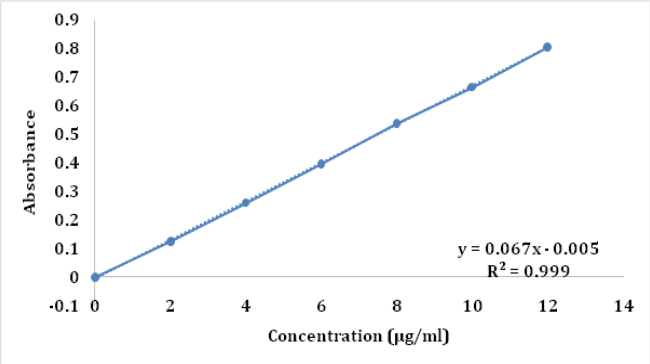


**Figure 3: Calibration curve of butorphanol tartrate**

### Validation of calibration curve method

### Linearity

Linearity of drug was established by response ratios of drug. Response ratio of drug calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio table 1.

**Table 1: Response ratio of butorphanol tartrate**

| S. No. | Butorphanol tartrate | | |
|---|---|---|---|
| | Conc. (µg/ml) | ABS | Response Ratio |
| 1. | 0 | 0 | 0 |
| 2. | 2 | 0.125 | 0.062 |
| 3. | 4 | 0.260 | 0.065 |
| 4. | 6 | 0.397 | 0.066 |
| 5. | 8 | 0.537 | 0.067 |
| 6. | 10 | 0.665 | 0.066 |
| 7. | 12 | 0.806 | 0.067 |

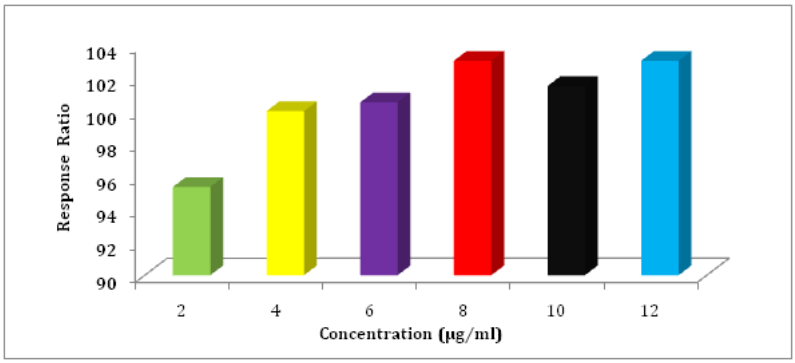


**Figure 4: Response ratio curve of butorphanol tartrate**

### Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of raloxifene to preanalysed tablet solutions. The resulting solutions were then re-analysed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels table 2.

**Table 2: Results of recovery studies**

| Recovery Level % | % Recovery (Mean±SD)* |
|---|---|
| 80 | 100.02±0.103 |
| 100 | 100.01±0.051 |
| 120 | 100.17±0.316 |

### Precision

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to Day and analyst to analyst) and reproducibility. Repeatability was performed by analyzing same concentration of drugs for five times. Day to Day was performed by analyzing 5 different concentration of the drug for three days in a week. The results are shown in table 3.

**Table 3 Results of precision (%R.S.D.)**

| Parameter | | Mean±SD |
|---|---|---|
| Precision (%R.S.D.)* | Repeatability | 99.06±0.036 |
| | Day to Day | 98.81±0.021 |
| | Analyst to Analyst | 98.83±0.027 |
| | Reproducibility | 99.74±0.56 |

### Limit of detection (LOD) & limit of quantification (LOQ)

Table 4 shown the result of LOD & LOQ of butorphanol tartrate by UV spectrophotometric method, according to ICH guideline which was shows limit of detection (LOD) was 0.1019µg/ml and LOQ value was 0.3089µg/ml for butorphanol tartrate at 278 nm.

**Table 4: Result of LOD & LOQ**

| | Butorphanol Tartrate |
|---|---|
| | at 278 nm |
| **LOD** | 0.101938 µg/ml |
| **LOQ** | 0.308902 µg/ml |

### Robustness

As per ICH norms, small, but deliberate variations in concentration of the mobile phase were made to check the method's capacity to remain unaffected. The ratio of mobile phase was change from, 0.05M Sulfuric acid: distilled water (70:30; %v/v) to (75:25 % V/V).Result of robustness are reported in table 5.

**Table 5: Result of Robustness**

| CONC. / REP | Concentration found (µg/ml) | | | | |
|---|---|---|---|---|---|
| | **2** | **4** | **6** | **8** | **10** |
| Replicate-1 | 1.95 | 3.95 | 6.02 | 8.98 | 9.98 |
| Replicate-2 | 1.96 | 3.98 | 5.98 | 8.95 | 9.86 |
| Replicate-3 | 1.99 | 3.90 | 5.99 | 8.95 | 9.68 |
| Replicate-4 | 1.89 | 4.01 | 5.98 | 8.96 | 9.78 |
| Replicate-5 | 1.99 | 3.96 | 5.95 | 8.95 | 9.98 |
| Mean | 1.89 | 3.96 | 5.98 | 8.96 | 9.88 |
| % Mean | 97.80 | 99.66 | 99.91 | 99.82 | 99.52 |
| SD | 0.041 | 0.040 | 0.023 | 0.021 | 0.026 |
| **% RSD** | **0.021** | **0.010** | **0.038** | **0.023** | **0.020** |
| | | | | **Mean % RSD** | **0.022** |

**Analysis of tablet sample**

Twenty marketed tablets of butorphanol tartrate were weighed and ground to a fine powder; amount equal to 10 mg of butorphanol tartrate was taken in 100 ml volumetric flask and sonicated for about 10 min to solubilized the drug present in tablet powder and the volume was made up to the mark with 0.05M sulfuric acid: distilled water (70:30; %v/v). After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with 0.05M sulfuric acid: distilled water (70:30; %v/v) to get the final concentrations of drug in the working range. The absorbances of final dilutions were observed at selected wavelengths and the concentrations were obtained from calibration curve method. The procedure was repeated for five times table 6.

**Table 6: Analysis of tablet formulation**

| S. No. | Absorbance | Conc. found (µg /ml) | Amount claimed per tablet (mg) | Amount found per tablet (mg) |
|---|---|---|---|---|
| | 278 nm | Conc. | | |
| 1. | 0.665 | 9.95 | 10 | 9.95 |
| 2. | 0.662 | 9.90 | 10 | 9.90 |
| 3. | 0.660 | 9.87 | 10 | 9.87 |
| 4. | 0.665 | 9.95 | 10 | 9.95 |
| 5. | 0.662 | 9.90 | 10 | 9.90 |
| 6. | 0.665 | 9.95 | 10 | 9.95 |
| | | | Mean | 9.92 |
| | | | S.D. | 0.34641 |
| | | | %R.S.D. | 0.003492 |

## CONCLUSION

The results and the statistical parameters demonstrate that the proposed UV spectrophotometric method is simple, rapid, specific, accurate and precise. Therefore, this method can be used for the determination of butorphanol tartrate either in bulk or in the dosage formulations without interference with commonly used excipients and related substances.

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