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DEVELOPMENT OF UV-SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF METHYL SALICYLATE FROM TRANSDERMAL PATCH

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Abstract: Transdermal Drug Delivery System are topically applied medications in the form of patches that are intended to deliver a therapeutically effective dose of a drug across the patient's skin at a controlled rate for systemic effect. Transdermal patches are now available for a wide range of pharmaceuticals. Methyl Salicylate is used in topical treatment and high-dose dermal patch, to relive pain of minor aches and pains of muscle and joints associated with arthritis. In the present study a simple, sensitive, rapid, accurate and precise spectrophotometric method has been developed for the estimation of methyl salicylate in transdermal patch. Methyl Salicylate shows maximum absorbance at 270 nm. Beer's law was obeyed in the concentration range 2-45 µg/ml. The limit of detection and limit of quantification were found to be 0.48 and 1.48 µg/ml, respectively. Results of analysis were validated statistically and by recovery studies. The method was validated as per ICH guideline in terms of linearity, accuracy (recovery study), precision, limit of detection, limit of quantification. The method was successfully applied to determine content of methyl salicylate from transdermal patch.

Keywords: Transdermal patches, arthritis, spectrophotometric method, limit of detection and limit of quantification, linearity, recovery study.

I. INTRODUCTION

The oral route is the most prevalent method of medication delivery. The advantages and disadvantages of this mode of administration include first-pass metabolism, drug breakdown in the gastrointestinal system due to enzymes, and pH. A unique medication delivery mechanism was designed to solve these challenges. The term "Transdermal Drug Delivery System" refers to drug delivery through the skin to generate a systemic effect of a medicine. These are dosage forms in which the drug is delivered to viable epidermal and/or dermal tissue of the skin for a local therapeutic impact, while a large portion of the drug is carried into the systemic blood circulation. Transdermal drug delivery systems are now one of the most promising drug delivery technologies. Transdermal drug delivery has an advantage over injectable and oral drug delivery in that it improves patient compliance and avoids first-pass metabolism. Transdermal Drug Delivery System not only permits continuous input of drug with short biological half-life also avoids pulsed entry into systemic circulation, which can produce unwanted side effects**.**

Methyl salicylate, also known as Oil of winter green, is chemically methyl-O-hydroxy benzoate (Fig. 1) with molecular weight 152.149 g/mol and act as an active ingredient in many topical analgesic preparations. The molecular formula of methyl salicylate is C8 H8 O3. it acts as A counterirritant, a substance which creates irritation or mild inflammation in one location with the goal of

lessening discomfort and inflammation in another location. It may cause analgesic (pain relief) and anti-inflammatory effects by inducing vasodilatation thereby increasing blood flow and temperature to the localized area of tissue.

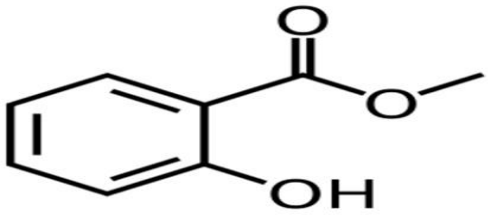


Figure No.1. Structure of Methyl Salicylate

Analytical methods are classified as non-instrumental and instrumental. Different instrumental methods involve spectroscopy, chromatography, mass spectroscopy, Calorimetry, microscopy, electrochemistry, environmental analysis, forensic, crystallography, etc.(Gaurav) Spectrophotometric measurements are applied in number of different ways such as inorganic, analytical and pharmaceutical chemistry. Quantitative estimation of UV-visible absorption at particular wavelength can be used to ascertain the quantity of molecular species absorbing the light. The ever-increasing number of medications and drug combinations on the market necessitates the development of analytical tools for monitoring their quality. The procedures must be developed in such a way that they take less time to design and produce the most accurate and robust results possible. The current study dosage form comprises nabumetone in solid oral dosage forms, which was recently approved by the USFDA. The goal of this project is to develop and validate a simple, precise, accurate, and cost-effective RP-HPLC technique for the estimation of nabumetone in bulk and pharmaceutical dosage forms that follows ICH recommendations.

2. MATERIALS AND METHODS

2.1. Chemicals and reagents

The API Methyl salicylate used for the method development is procured from New Modern Chemical Corporation, Mumbai. The solvents Methanol (80%) and acetonitrile (20%) are bought from Thermosil Fine Chem Industries, Pune and SDFCL s d Fine Chem Limited, Mumbai respectively.

2.2. Selection of wavelength

The pattern changed into scanned from 200-400 nm in a 1 cm cell and spectra were recorded. The wavelength selected for the further study is 237 nm.

2.3 Instruments

Table 1. Instruments used in work

Sr. No.	Equipment	Specification
1	UV spectrophotometer	UV-1800, Shimadzu Corporation, Japan
2	FTIR	IR Affinity -1 Shimadzu, Japan
4	Digital magnetic stirrer	Remi Motors, Mumbai
5	Digital Balance	Model No AW-220 and BX-6205 Pioneered (OHAUS), USA

2.4 Spectrophotometric Conditions:

- Mode: Spectrum
- Measuring Mode: Absorbance
- Wavelength Range: 200 nm to 400 nm

2.5 Preparation of Standard Stock Solution

Solution A. 1 ml of Methyl Salicylate is dissolved 10 ml of Methanol : Acetonitrile (80:20) it gives 10 ug/ml.

Solution B. 1 ml of Solution A is diluted to 10 ml of solvent

Solution C. 1 ml of Solution B were diluted to 10 ml of solvent.

2.6 Validation of A Method for Analysis of Methyl Salicylate

a) Accuracy

Accuracy expresses the closeness or agreement between the measured value and an accepted or true value. Accuracy was calculated at three different levels in terms of % recovery by standard addition method by adding the known amount of drug separately to the pre- sample at three different concentrations (80%, 100% and 120%) of assay concentration and percentage recoveries are calculated.

b) Precision

Precision of the analytical method is expressed as the S.D. or R.S.D of the series of measurement. It was ascertained by replicate estimation of the drugs by proposed method for marketed formulation.

c) Linearity

Linearity determination is usually conducted in order to justify that single point calibration and may be applied when the method is used for routine analysis. The justification requires demonstration whose responses are linear over the range of interest and if extrapolated back to zero concentration on the X-axis, the intercept passes through the origin.

d) Limit of Detection (LOD)

LOD is the lowest concentration of analyte in a sample matrix that is detected, although not necessarily quantitated under specific analytical condition It is the limit test that specifies whether or not an analyte is above or below a certain value. LOD may be calculated based on the standard deviation (SD) of the response and the slope(S) of the calibration curve at levels approaching the LOD according to the formula:

The limit of detection (LOD) may be expressed as:

$$\mathbf{LOD = 3.3\ X\ \frac{\sigma}{S}}$$

e) Limit of Quantitation (LOQ)

LOQ is the smallest amount of analyte in a sample matrix that can be quantified with acceptable accuracy and precision. LOQ is also type of sensitivity.

The limit of quantitation (LOQ) may be expressed as:

$$\mathbf{LOQ = \frac{10\,\sigma}{S}}$$

Where,

σ standard deviation of the response,

S slope of calibration curve of analyte

f) Ruggedness

Ruggedness is a measure of reproducibility of test results under normal and expected operational conditions from analyst to analyst and instrument to instrument.

Experimental work & Results

FTIR SPECTRAL STUDIES

FTIR spectrum of drug was recorded on an Infrared spectrophotometer (Shimadzu).

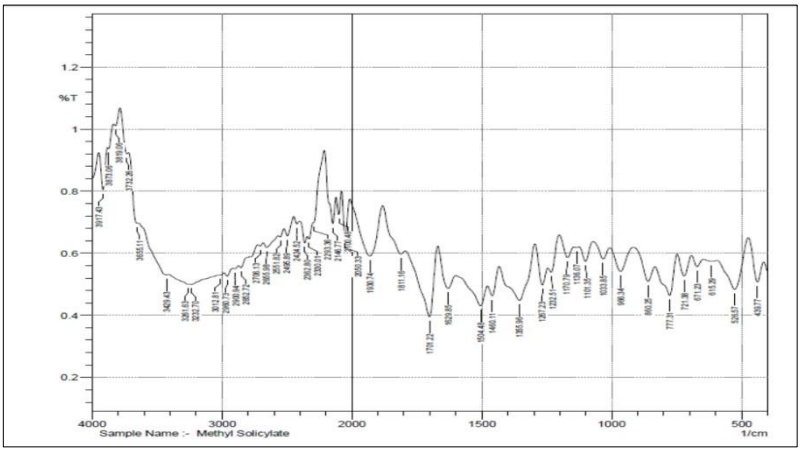


Figure No.2: FTIR of Methyl Salicylate

1. Study of spectra, selection of scanning range and detecting wavelength

Solution C. is scanned in a 1 cm cell in the range of 400-200 nm and spectra were recorded. The wavelength selected for the further study is 237 nm.

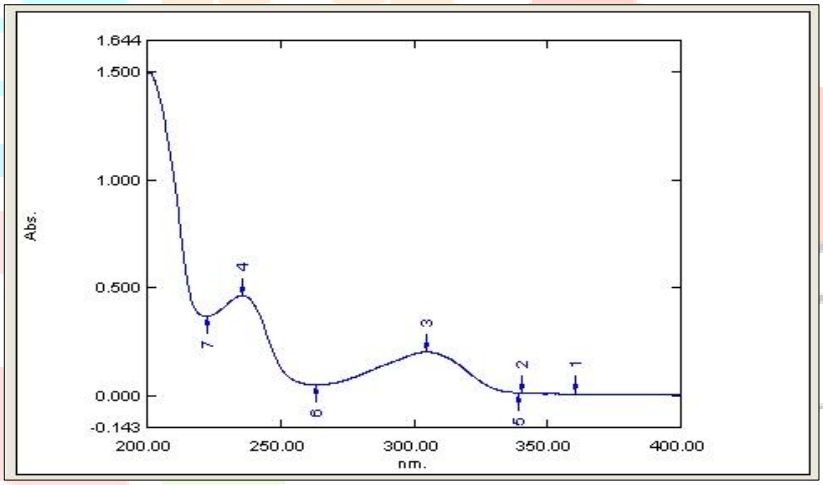


Figure No.3: UV – Spectra of Methyl Salicylate

2. Study of Beers- Lamberts Law

The dilutions ranging from 2 ug/ml – 45 ug/ml are prepared from the Solution C. all the solutions were scanned in spectrum mode over the range of 400 – 200 nm against Methanol : Acetonitrile (80:20) blank.

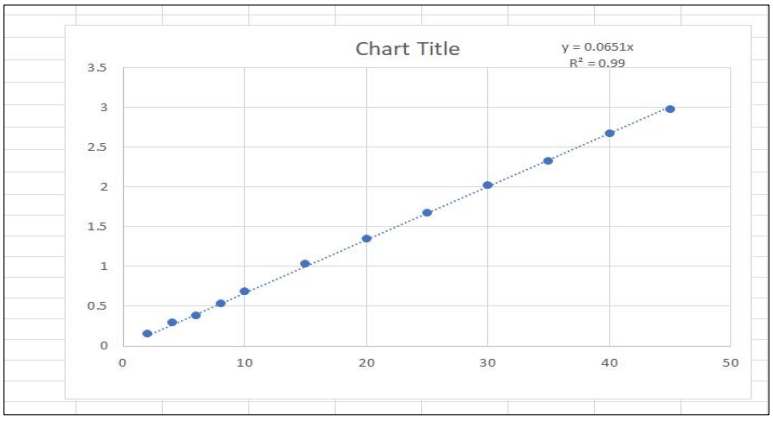


Fig.No.4: Beer – Lamberts Law study for Methyl Salicylate

3. Determination of absorptivity, A(1%, 1cm) values at selected wavelengths

Five different standard solutions were prepared and they were appropriately diluted. Absorbance of each of standard solution was measured at 237 nm in a 1 cm cell against Methnol:Acetonitrile (80:20) as blank.

A (1%, 1cm) values were calculated using following formula

$$\text{A (1\%, 1cm)} = \frac{\text{Absorbance}}{\text{Concentration}\left(\frac{\text{g}}{\text{ml}}\right)}$$

Table 2: **A (1%, 1cm) Determination of Absorptivity**

Sr. No.	Methyl Salicylate (237 nm)
1	694.3
2	693.9
3	694.5
4	694.5
5	692.9
Mean ± S.D.	**694.02 ± 0.4520**

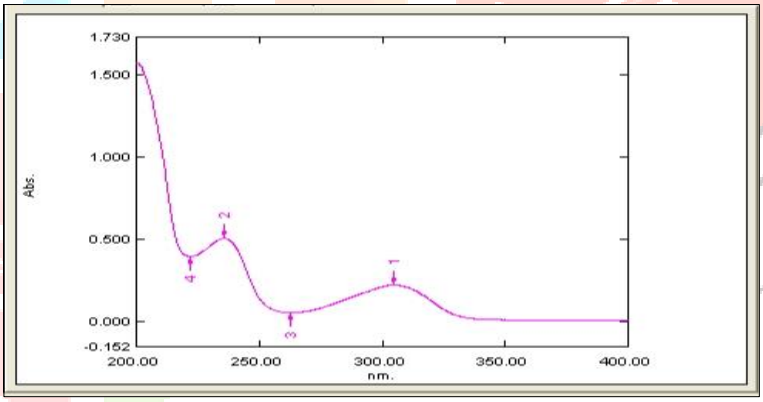
4. Application of proposed method to marketed preparation

Details of marketed Formulation

Trade Name: VIOPATCH

MFG: UNEXO Life Sciences

UV- Spectrophotometric Calibration of MS Patch



Fig,No.5: UV Spectra of marketed formulation

Recovery studies

It was carried by standard addition method.

Sample solution

Accurately weighed quantities of pre-analyzed patchs-content equivalent to 10 mg MS was taken in series of 10.0 mL volumetric flasks and to then known amount of MS were added at different concentration levels so as to produce solutions containing 80%, 100% and 120% of the label claim. The contents in the flasks were shaken with methanol:Acetonitrile and volumes were made up to the mark. The solutions were filtered through whatman No. 1 filter paper. An accurately measured 1.0 ml. portion of each filtrate was diluted to 10.0 mL with methanol:Acetonitrile. The absorbance of resulting solutions was measured at 237 nm against methanol:Acetonitrile as blank.

Percentage recovery was calculated as follows,

$$\% \text{ Recovery} = \frac{\text{Total drug estimated} - \text{Amount contributed}}{\text{Amount of pure drug added}} \times 100$$

Table 3: Observation results and statistical data for recovery study

Component	Label Claim	Amount of standard drug added (ug)	% Recovery
Methyl Salicylate	9.985	0	99.85
	9.956	8	99.56
	9.980	10	99.80
	9.985	12	99.85
		Mean	**99.7650**
		±S.D.	**0.138684**
		CV	**0.01923**
		RSD	**0.139011 %**

VALIDATION

a) Accuracy

Accuracy was calculated at three different levels in terms of % recovery by standard addition method by adding the known amount of drug separately to the pre- sample at three different concentrations (80%, 100% and 120%) of assay concentration and percentage recoveries are calculated. The results are shown in **Table 3**

b) Precision

Precision of the analytical method is expressed as the S.D. or R.S.D of the series of measurement. It was ascertained by replicate estimation of the drugs by proposed method for marketed formulation.

The results are shown in **Table 4**

Table 4: Observations and results of marketed formulation analysis

Sr. No.	Laboratory mixture	Wt. of Patch	Amt estimated in Avg wt. of patch	% label claim
1	Standard	10	9.985	-
2	Sample 1	2.74	9.982	99.82
3	Sample 2	2.55	9.975	99.75
4	Sample 3	2.61	9.956	99.56
5	Sample 4	2.88	9.985	99.85
6	Sample 5	2.65	9.965	99.65
			Mean	**99.72**
			CV	**0.145300**
			±S.D.	**0.120540**
			R.S.D.	**0.120872%**

c) Linearity and range.

According to ICH, patch equivalent to 80%, 90%, 100%, 110%, 120% of label claim is to be taken and diluted appropriately to obtain a concentration in the range of 80% - 120% of test concentration. The absorbance of final solution was read at 237 nm and a graph was plotted as % test concentration Vs absorbance and is shown in Figure No. 6.5. MS in marketed formulation were found to be linear in the range ± 20% of the test concentration.

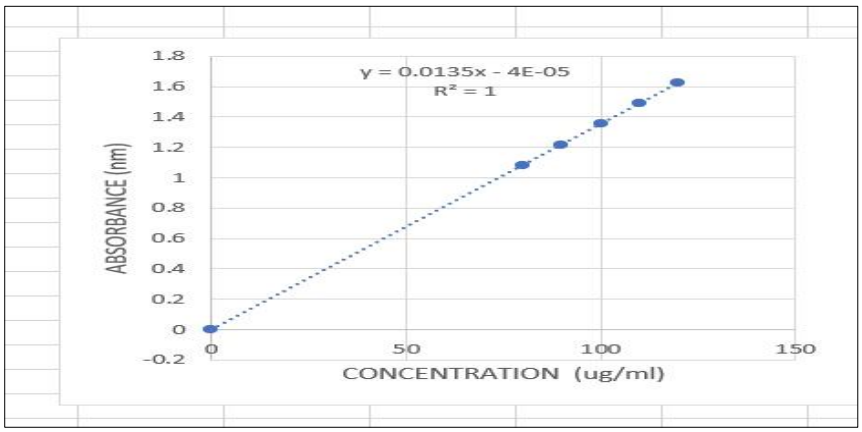


Fig. No.6: Linearity curve of marketed formulation

d) Limit of Detection (LOD)

$$\text{LOD} = 3.3 \text{ X } \frac{\sigma}{S}$$

e) Limit of Quantification

$$\text{LOQ} = \frac{10\,\sigma}{S}$$

Where, σ standard deviation of the response,

S slope of calibration curve of analyst

Table 5: Linear Regression Analysis

Parameters	MS 237 nm
Linearity Range	2-45 ug/ml
Slope	0.0662
Intercept	0.21432507
Correlation Coefficient (R^2)	0.9997
LOD (ug/ml)	0.48
LOQ (ug/ml)	1.48

f) Ruggedness

The ruggedness of the method was studied under three different parameters. Samples were prepared as per marketed formulation estimation.

ii) Intraday variation

The samples were analyzed on different times on same day by proposed method. The percent labeled claim was calculated and results of estimation are shown in **Table 6.**

Table 6: Results and statistical data for Intraday study

Time	Absorbance	% Label Claim
Time 1	0.694	99.85
Time 2	0.694	99.85
Time 3	0.695	100.0
	Mean	**99.90**
	±S.D.	**0.0866025**
	C.V.	**0.0075**
	R.S.D.	**0.0866892 %**

ii) Interday variation

The samples were analyzed by proposed method on three different days (1st, 2nd and 3rd day). The percent labeled claim was calculated and results of estimation are shown in **Table 7**.

Table 7: Results and statistical data for Interday study

Days	Absorbance (237 nm)	% Label Claim
Days-1	0.695	100.0
Day-2	0.694	99.85
Day-3	0.696	100.14
	Mean	**99.99**
	±S.D.	**1.145029**
	C.V.	**0.021033**
	R.S.D.	**0.145034 %**

iii) Different Analyst

The samples were analyzed by three different analysts as per the proposed method. The percent labeled claim was calculated and results of estimation are shown in **Table 8**.

Table 8: Results and statistical data for Different Analyst study

Analysts	Absorbance (237 nm)	% Label Claim
Analyst-1	0.693	99.71
Analyst-2	0.694	99.85
Analyst-3	0.696	100.14
	Mean	**99.90**
	±S.D.	**0.219317**
	C.V.	**0.04810**
	R.S.D.	**0.2195337 %**

Conclusion

From all above results, it have been concluded that the developed UV- Spectrophotometric method for the estimation of drug from transdermal patch formulation has obliged the ICH guidelines. As per the ICH guidelines, the developed method has complied the linearity range (calibration data), accuracy/drug recovery studies (%), precision studies and robustness.

Due to high sensitivity and simple sample preparation can be the part of undergraduate curriculum. Moreover spectrophotometric methods have obvious advantages over sophisticated instrumental analysis. Hence simple, economical and less time consuming spectrophotometric methods always have a role in routine pharmaceutical analysis.

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