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SPECTROPHOTOMETRIC AND CHROMATOGRAPHIC METHODS FOR THE ESTIMATION OF MESALAMINE: A BRIEF REVIEW

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ABSTRACT

Anti-inflammatory agents are the important class of drugs used in various commercial pharmaceutical formulation for the treatment of fever, inflammation and minor pain.one of the important anti-inflammatory drug is Mesalamine which belongs to the class of Amino-salicylic acid derivatives. Mesalamine is a bowel specific anti-inflammatory drug used in the treatment of inflammatory bowel diseases such as ulcerative colitis and Crohn's disease.it is available in different pharmaceutical dosage forms such as delayed release, extend release and enteric coated tablets and capsulesetc., The several of Mesalamine brand's available in market are Apriso, Asacol MR-400mg, Lialda, Pentasa-500mg, Asalosa-800 etc. Hence routine quality control of Mesalamine in these pharmaceutical dosage form requires effective analytical procedures. In this present review an extensive survey of research work published in various research journals has reviewed and found that various instrumental analytical methods were developed, validated and used for the estimation of Mesalamine in bulk drug and formulation. The developed analytical methods include Spectrometric such as Ultraviolet (UV) and Visible; Spectroflourimetric and Chromatographic methods such as High Performance Liquid Chromatographic (HPLC), Reverse Phase High Performance Liquid Chromatographic (RP-HPLC), Ultra Performance Liquid Chromatographic (UPLC).

Keywords: *Mesalamine, Spectrophotometry, Chromatography, Anti-inflammatory, Estimation.*

INTRODUCTION

Mesalamine [1, 2] is a 5-amino-2-hydroxy benzoic acid belongs to the class of amino salicylate anti-inflammatory agent used for the treatment of inflammatory bowel disease including ulcerative colitis, inflammed anus or rectum and to maintain remission in chron's disease. It is also known as Mesalazine. It acts by inhibiting mucosal production of arachidinic acid metabolites through cyclooxygenase and lipooxygenase pathways and also inhibition of prostaglandins in colon [3]. Its oral bioavailability is 20-30% and the rectal bioavailability is 10-35%. It rapidly and extensively gets metabolised in liver and intestinal mucosal wall [4].

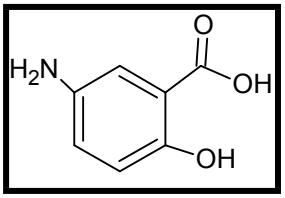

Fig. 1: structure of Mesalamine

As Mesalamine is available in several brands in pharmaceutical dosage forms, the quality control of formulation containing mesalamine plays a vital role in drug industries**.** The reason being, these formulations may contain impurities, related substances, degraded products and toxic substances along with the drug contents, which may cause the harmful pharmacological effect in patients. Hence, to launch such formulations in the market they have to be analysed for their purity and drug contents. Keeping this in view various analytical tools such asUltraviolet (UV) and Visible-spectrophotometry, Spectroflourimetric and Chromatographic methods; High Performance Liquid Chromatographic (HPLC), Reverse Phase High Performance Liquid Chromatography (RP-HPLC) and Ultra Performance Liquid Chromatography (UPLC) were developed for the estimation of mesalamine and same were reviewed briefly in the present communication.

Sama NS *et al.,* have reported the spectrophotometric determination of Mesalamine in bulk and pharmaceutical preparations by adapting two methods (A and B). Method A was reported based on the reaction between mesalamine with 1, 2-Napthaquinone-4-sulphonate (NQS) in the presence of NaOH which shows absorption maxima at 475nm. Simillarly Method B was developed based on the reaction between mesalamine with acidic solution of *p*-dimethyl amino cinnamaldehyde (PDAC) which forms reddish brown colour and was measured by UV spectrophotometer at 524nm. A linearity concentration range of 1.0-16.0µg/ml was found for method A, also concentration range of 5-25.0µg/mlfor method B. Percentage recovery of mesalamine was found to be 96.6% for method A. and 98.0% for method B respectively. However Percentage RSD value was reported as 0.4177% and 0.395% for method A and B respectively [2].

Moharana AK *et al.,* have reported a simple and cost effective spectrophotometric method for the estimation of Mesalamine in pure form and in pharmaceutical formulations. The absorbance value at 303nm was used for the estimation of Mesalamine and obeyed Beer's law in the concentration range of 10-50µg/ml [5].

Reddy MP *et al.,* have developed a quantitative estimation method for Mesalamine in bulk sample and its pharmaceutical dosage forms by two simple spectrophotometric methods. Method A was based upon the diazotization of primary amine group of mesalamine with sodium nitrite and concentrated HCl followed by coupling reaction with resorcinol to form orange coloured chromogens which shows absorption maximum absorption at 460nm. Method B was based on the reactions between mesalamine and vaniline in acidic medium producing schiff's base having absorption maxima at 395nm [6].

Darak V *et al.,* have published a report on the derivative spectroscopic determination of Mesalamine in commercial tablet formulation by two methods. Mesalamine has absorption maxima at 325.4nm by Method A and 310nm by Method B respectively in 0.1N

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NaOHas solvent. The methods were validated statistically in the concentration range of 5-25µg/ml [7].

Darak VR *et al.,* have developed three colorimetric methods for the determination of Mesalamine in bulk drug and pharmaceutical preparations. The absorption maxima for the methods A and B were found to be 510.5nm and 522.5nm with concentration range of 2-10µg/ml respectively based on the oxidation reaction of Mesalamine followed by complexation of iron with 1,10-phenanthroline, 2,2-bipyridine which forms red chromogens. The method C was based upon reaction between Mesalamine with B-Methyl benzothiazolinone hydrate which form green colored chromogen which shows absorption maxima at 586.8 nm with concentration range of 4-20µg/ml [8].

Zadeh HA *et al.,* have a developed spectroflourimetric method for the Determination of Mesalamine in human serum using solid phase extraction sorbent (SPE) for separation and pre concentration of trace amount of Mesalamine was assisted using column methodand the retained analyte was eluated with NaOH solution and the concentration of eluated mesalamine was then spectroflourimetrically determined at maximum wavelength 480nm with excitation at 340nm.the limit detection and enrichment factor were 0.04 and 40µg/L respectively. The relative standard deviation (RSD) resulting from analysis of six replicates 100ml solution containing 1.0µg/L Mesalamine was 2.05%. This optimized method was successfully applied to the determination of mesalamine in blood serum samples [9].

Patel KM *et al.,* havecarried out the development and validation of spectrophotometric methods for the estimation of Mesalamine in tablet dosage form by employing three different methods A, B, C which were based upon the formation of colored chromogens. The wavelength at which absorbance measured was at 552nm, 440nm and 494nm respectively for all the three methods A, B, C [10].

Sabha TN*et al.,* have been a developed a simple, accurate and more sensitive spectrophotometric method for the determination of Mesalamine by using sodium nitroprusside as chromogenic agent which forms green coloured chromogen. The visible detection was carried out at 703nm. The linearity concentration range was found to be 0.0-30µg/ml with molar absorptivity of 2.0367×10^4 l/mol/cm. The average recovery and % relative standard deviation were reported as 103.0% and 1.5% respectively [11].

Narala SR *et al.,* have developed two different spectroscopic methods for the development and validation of Mesalamine in pharmaceutical preparation. Method A involved the formation of yellow colored chromogen by the reaction between Mesalamine and*p*-hydroxy benzaldehyde to form schiff's base which showed absorption maxima at 420nm (concentration range; 8-28µg/ml). Method B was based upon the reaction of Mesalamine with Folin ciocalteu phenol's reagent under alkaline condition forming blue colored chromogens which shows absorption maxima at 725nm and obeyed Beer's law concentration range within 4-24µg/ml [12].

Zakaria RA, have developed two visible spectrophotometric methods for the estimation of Mesalazine in bulk drug and capsule formulations. The method A was based on the oxidative coupling reaction of Mesalazine with 8-hydroxy Quinazoline which exhibited absorption maxima at 644 nm within concentration range of 10-300µg/ml. However Method B was based on the reaction of Mesalazine with N-(1-napthyl) ethylenediamine which showed maximum absorption at 543nm. The % RSD was fund to be ±1.31% - ±0.39% and ±0.88% - ±0.32% for methods A and B respectively [13].

Chandra BS *et al.,* have developed spectrophotometric methods (A, B, C) for the estimation of Mesalazine in bulk and tablet dosage forms. Mesalazine was estimated in the concentration range of 1-30, 1-15 and 2-30 µg/ml in methods A, B and C respectively [14].

Singh RK *et al.,* have reported UV spectrophotometric methods for the Mesalazine estimation in pharmaceutical dosage forms. Methanol was used as solvent and the absorption maximum was found to be 210nm. The linearity concentration range was reported as 0.2- 50 µg/ml [15].

Darak VR *et al.,* have developed and validated visible spectrophotometric methods (A, B, C) for the determination of Mesalamine in pharmaceutical dosage form. The method A and B were based on the formation of coloured chromogens with absorption maxima at 440nm and 523.5 nm with a linearity concentration range of 50-250µg/ml and 200-100µg/ml respectively. The absorption maxima for the method C was found to be 616nm with a linearity concentration range of 10-50µg/ml [16].

Zakaria RA, has a developed spectrophotometric method for the determination of Mesalazine by diazotization coupling method in methanol. The absorption maxima was found to be 471nm, which obeyed Beer's law in the concentration range of 10-300 µg/ml with a molar absorptivity of $2.9480 * 10^4$ $l.mol^{-1}cm^{-1}$ sandell sensitivity index of $0.005\mu g/cm^2$.The relative error was reported in the range of -0.96 to -0.23% with relative standard deviation of ± 1.05 to ± 0.37% [17].

Rao RN *et al.,* have developed and validated an UV Spectrophotometric method for the determination of Mesalazine in pure and tablet dosage form. The solvent used was phosphate buffer with pH 6.8 and maximum absorbance was found to be 330nm [18].

Madhavi V *et al.,* have reported an efficient spectrophotometric method for the determination of Mesalazine in bulk and tablet dosage form based on diazocoupling reaction with resorcinol .The absorption maxima for the coloured compound was found to be 490nm in the concentration range of 2-20µg/ml,and obeyed Beer's law [19].

Gatkal SH et *al.*, have developed UV-visible spectrophotometric method for the kinetic degradation study of Mesalamine by dry heat degradation carried out at$50^{0,}$ 60^0,70^{00}C. Distilled water was used as solvent. The concentration range was found to be 2-16µg/ml. The energy of activation was estimated as 0.05169Joule/mol. This method showed high sensitivity with good l [20].

Garmonov SY et *al.,* have developed a spectrophotometric method determination of Mesalazine in urine by using 7-Chloro-4, 6-dinitrobenzofuraxaneas an analytical reagent. The absorbance of Mesalazine with p^H 6-8 was estimated at 500nm. The limit of detection for Mesalazine was found to be 0.31µg/ml. the developed method was successfully adapted for accessing Mesalazine acetylation in metabolic process of individual human phenotypes[21].

Elbashir AA *et al.,* have developed a method for the spectroflourimetric determination of Mesalazine in pharmaceutical formulation. Water was used as solvent and the fluorescence intensity was measured at an excitation wavelength of 298nm and emission wavelength of 410nm, which obeyed the Beer's law in the linearity concentration range of 0.1-0.9µg/ml [22].

Reddy KS *et al.,* have reported simple, precise and accurate RP HPLC assay method for the estimation of Mesalamine in bulk and its tablet dosage form. The mobile phase used composed of mixed buffer and acetonitrile (65:35v/v) required for effective separation using waters HPLC C18, 100 × 4.6, 5µ column with a flow rate of 1.0 ml/min for UV detection at 258nm. The retention time for Mesalamine was found to be 3.214mins within the concentration range of 10-60µg/ml with a correlation co-efficient 0.998. The proposed method was validated as per ICH guidelines and successfully applied for routine analysis of Mesalamine in bulk samples and its formulations [23].

Rao KH *et al.,* have developed and validated RP-HPLC method for the estimation of Mesalamine in bulk and tablet dosage form using Xterra ODS C18 (250 mm × 4.6mm I.D., 5 µm particle size) column at ambient temperature. The UV detection was carried out at 235nm with a flow rate of 20µL. The mobile phase used was composed of phosphate buffer p^H 6.8: methanol (60; 40, v/v). The retention time was found to be 2.172 min and the percentage recovery was reported within the range of 98.0% and 101.3% [24].

Gatkal SH *et al.,* reported development and validation of stability indicating HPLC method for determination of Mesalamine in solid pharmaceutical dosage form. The chromatographic method was achieved by using analytical C-18 Reverse column (250mm × 4.6mm) employing mobile phase of water: methanol in the ratio of 80:20v/v with UV detection. The linearity concentration range was found to be 10-60µg/ml with a correlation co-efficient 0.999. The %RSD values were reported as less than 2% [25].

Moharana AK *et al.,* have developed and validated RP-HPLC method for the determination of Mesalamine. The detection was carried out using mobile phase composed of methanol: water (50:50v/v) by employing C-18 (4.6mm × 2.5cm) at a flow rate of 0.5ml/min. The retention time was found to be 3.070 min. The linearity concentration was reported as 20-50µg/ml with a percentage recovery of 99.77%. This proposed method was precise, accurate, selective and rapid for the determination of Mesalamine at QC levels [26].

Nobilis M *et al.,* have developed HPLC method for the determination of Mesalamine and its metabolite in blood plasma. The chromatographic methods were developed by using 250.4mm column containing purospher RP-18 e, 5µm with a pre-column (4-4mm). The column effluent was monitored by employing UV photodiode array and fluorescence detector at the wavelength of

313nm and 300nm respectively. The flow rate was maintained at 1mL/min. this validated HPLC method was applied to pharmacokinetic study of Mesalazine in human and animals [27].

Kanubhai TR *et al.,* have reported gradient reverse phase UPLC method for thedetermination of Mesalamine related impurities from drug product. The chromatographic separation was done by employing BEH C_{18} column (50mm × 2.1mm, 1.7µm) using gradient elution with the detection wavelength at 220nm. The flow rate, column oven temperature, injection volume optimized at 0.7ml/min, 40^0 C and 7µl respectively. The %RSD value was reported as less than 2.0%. The method was validated as per ICH guidelines and was successfully applied for quantification of impurities and degradation products in Mesalamine delayed released formulation [28].

Darak V *et al.,* have developed and validated HPLC method for the estimation of Mesalamine in tablet dosage.Acetonitrile and water in the ratio of 60:40v/w was used as mobile phase by using RP C_{18} column with a flow rate of 0.6ml/min at 25 ± 1^0C. The effluent was detected at a wavelength of 330nm. The linearity concentration was found to be 20-100µg/ml and Retention time was found to be 3.09min for run time of five minutes [29].

Sahoo NK *et al.,* have developed and validated a stability indicating RP HPLC method for the determination of Mesalamine in bulk tablet dosage forms with UV visible detector employing phenomenex RP-C18 column. Methanol: water was used as mobile phase in the ratio of 50:50v/v. The flow rate of mobile phase was 0.9ml/min with the UV detection at 230nm with injection volume of 20µl. The linearity of Mesalamine was found to be 20-50µg/ml [30].

Rafael *et al.,* have developed HPLC, DPPH and Nitration methods for the determination of Mesalamine in pharmaceutical dosage form. The UV detection was carried out at 254nm by using C18 column using phosphate buffer of p^H 7.0 and methanol in the ratio 70:30 v/v as mobile phase. The DPPH method was carried out at 517nm using 100mmol/L acetate buffer of p^H 5.5, ethanol and 250mmol/L ethanolic solution of DPPH [31].

Gatkal SH *et al.,* have developed and validated stability indicating HPTLC method for the determination of Mesalamine in bulk drug and pharmaceutical dosage forms. The mobile phase composed of toluene: methanol: ethyl acetate in the ratio of 6.5:2.5:1 v/v were used as solvents for mobile phase by using precoated TLC aluminium plates with silica gel 60F-254. The UV detection was carried out at 244nm. The linearity concentration range was found in between the 200-600ng/band. The limits of detection and quantization were reported as 2.62 and 7.94 ng per spot respectively [32].

CONCLUSION

This review presents spectrophotometric, spectroflourimetric and chromatographic methods for the quantitative estimation of Mesalamine in bulk and pharmaceutical formulation. These methods were quite common and most frequently used for quantification or confirmation of substance identity and its purity in pharmaceutical industries and research laboratories.

REFERENCES:

1. www.drugbank.ca /drugs /DB00244.
2. Sama NS, Gurupadayya BM, Kumar CA. *J. Pharm. Res.,* **2011**; 4(1): pp 39-41.
3. www.rxlist.com /Lialda-drug / clinical pharmacology, htm.
4. https://en.wikipedia.org/wiki/mesalamine.
5. Moharana AK, Banerjee M, Panda S, Muduli JN. *Int. J. Pharm. Sci.,* **2011**; 3(2): pp 19-21.
6. Reddy MP, Prabhavathi P, Reddy NR, Reddy R. *Global Pharmacol.,* **2011**; 5(2): pp 101-105.
7. Darak VR, Karadi AB, Arshad MD, Patil D. *Cur. Pharm. Res.,* **2011**; 1(3): pp 232-235.
8. Darak VR, Karadi AB, Arshad MD, Raj SA. *Int. J. Pharm. Sci.,* **2011**; 2(4): pp 31-35.
9. Zadeh HA, kohansal S. *J. Braz. Chem. Soc.,* **2012**; 23(3).
10. Patel KM, Patel CN, Panigrahi B, Parikh AS, Patel HN. *J. Young Pharm.,* **2010**; 2(3): pp 284-288.
11. Sabah TN, Habeeb NN. *Eur. Chem. Bull.,* **2015**; 4(8): pp 384-388.
12. SR. Narala, K. Saraswathi. *J. Chem. Pharm. Res.,* **2011**; 3(1): 784-787.
13. Zakariya RA. *J. Raf. Sci.,* **2013**; 24(1): pp 146-158.
14. Chandra BS, Bhogela SS, Shaik M, Vadlamudi CS, Chappa M, Maddirala NS. *Quim. Nova.,* **2011**; 34(6): pp 1-11.
15. RK. Singh, PS. Patel, P. Gupta. *Int, J, Pharm, Sci, Res.,* **2010**; 1(3): 44-48.
16. Darak VR, Karadi AB, Arshad MD, Raju SA. *Der Pharma Chemica,* **2011**; 3(2): pp 342-346.
17. Zakariya RA. *J. Raf. Sci.,* **2009**; 20(1): pp 99-104.
18. Rao RN, Reddy LS, Reddy EP, Ravisankar Sulakshana S, Meenakshi R. *Int. J. Pharm. Res. Sch.,* **2015**; 4(4): pp 88-92.
19. Madhavi M, Panchakshari V, Prathyusha TN, Sekaran CB. *Int. J. Pharm. Sci. Rev. Res.,* **2011**; 11(1): pp 105-109.
20. Gatkal SH, Chopade VV, Mhatre PR, Chaudhari PD. *Int. J. Pharm. Chem. Sci.,* **2013**; 2(2): pp 978-981.
21. Garmonov SY, Nguyen ZC, Mingazetdinov IF, Yusupova LM, Shitova NS, Ismailova RN, Sopin VF. *Pharm. Chem. J.,* **2012**; 45(12): pp 757-760.
22. Elbashir AA, Abdalla FAA, Aboul-Enein HY. *Luminescence,* **2015**; 30(4): 444-50.
23. Reddy KS, Ramachandran B, NVS Naidu. *Int. J. Sci. Eng. Res.,* **2014**; 2(6): pp 52-56.
24. Rao KH, Rao AL, Sekhar KBC. *Int. J. Res. Pharm. Chem.,* **2013**; 3(2): pp 472-476.
25. Gatkal SH, Mhatre MR, Chopade VV, Choudhari PD. *Int. J. Pharm. Sci. Rev. Res.,* **2013**; 20(1): pp 200-204.
26. Moharana AK, Banerjee M, Sahoo CK, Sahoo NK. *Asian J. Pharm. Clin. Res.,* **2011**; 4(2): pp 71-73.
27. Nobilis M, Vybiralova Z, Sladkova K, Lisa M, Holcapek M, Kvetina J. *J. Chromatogr. A.,* **2006**; 11(19): pp 299-308.
28. Kanubhai TR, Muresh CP, Amith RK. *J. of Chem.,* **2011**; 8(1): pp 131-148.
29. Darak V, Karadi AB, Raju SA, Arshad MD, Ganure AL. *An. Int. J. Phar. Sci.*, **2012**; 3(1): pp 74-80.
30. Sahoo NK, Sahu M, Rao PS, Ghosh G. *J. Phme.,* **2013**; 12(3).
31. Rafael JR, Jabor JR, Casagrande R, Georgetti SR, Borin MF, Fonseca MJV. *Braz. J. Pharm. Sci.,* **2007**; 43(1): pp 97-103.
32. Gatkal SH, Mhatre PR, Chopade VV, Chaudhari PD. *Int. J. Pharm. Sci.,* **2013**; 2(2): pp 998-1004.

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