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ESTIMATION OF ALLOPURINOL – A REVIEW

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ABSTRACT

The present review article focuses on the estimation of Allopurinol and its combination of drugs by various analytical techniques. Allopurinol is used in the treatment of Gout and it acts by decreasing the uric acid levels in the blood. Allopurinol and a combination of a few drugs like flucytosine, α-lipoic acid, febuxostat, benzbromarone, oxypurinol, lesinuradare reviewed in this article. Estimation of the above-mentioned drugs by using various analytical tools like UV-Vis spectrophotometer, Ultra Performance Liquid Chromatography (UPLC), Liquid chromatography- Tandem mass spectrophotometry (LC-TMS), Hydrophilic- Liquid Interaction Chromatography (HILIC), High-Performance Liquid Chromatography (HPLC).

Key words: Allopurinol, Febuxostat, Benzbromarone, Chromatography, Hyperuricemia

INTRODUCTION

Gout is indeed a type of chronic inflammatory arthritis seen in adults. This disease is characterized by a higher concentration of serum uric acid (hyperuricemia) **[1]**. Allopurinol is worldwide the mainstay of modern treatment of gout and prevention of tumor lysis syndrome. Allopurinol an isomer of hypoxanthine, and its active metabolite oxypurinol (alloxanthin) act by inhibiting xanthine oxidase, an enzyme which forms uric acid (urate) from xanthine and hypoxanthine. Allopurinol can be administered either orally or intravenously. The oral bioavailability is about 67 to 90% with a peak plasma concentration occurring within one hour; the volume of distribution is approximately 1.6 L/kg **[2]**. Allopurinolis chemically 1*H*-pyrazolo[3,4-*d*] pyrimidin-4-ol and 1,5-dihydro-4*H*-pyrazolo[3,4-*d*]

pyrimidin-4-one. Allopurinol is a white or almost white, crystalline powderhaving a molecular weight of 136.11 g/mol **[3]**. Due to its therapeutic importance, the quantitative determination of Allopurinol in pharmaceuticals has considerable significance in quality control. Methods developed to determine Allopurinol in active pharmaceutical ingredients, dosage forms,and bio-samples are reviewed in the present article.

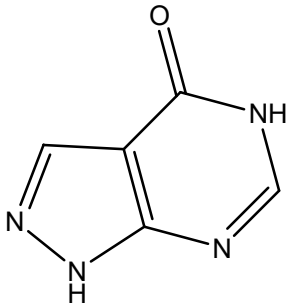

Figure 1: Allopurinol

METHODS FOR ESTIMATION

UV Spectrophotometric methods

Various UV spectrophotometric methods for Allopurinol single and in combination with other drugs are developed and are listed in **(Table 1)**.

Chromatographic methods:

Various chromatographic methods like UPLC, LC-TMS, HPLC was developed for estimation of Allopurinol in single and combination with other drugs. Methods for estimation of UPLC, LC-TMS, and HPLC are listed in **(Table 2, 3, 4)**.

Table 1: Methods for estimation of Allopurinol single and combination with other drugs by UV Spectrophotometry

S.NO	Drugs	Application	Description	Reference
1.	Allopurinol And Flucytosine	In pharmaceutical formulation	Detection wave length: Allopurinol: 281 nm Flucytosine: 275 nm Solvent: Allopurinol: 0.1M NaoH Flucytosine: 0.1M HCl Linearity range:0.25-3.5 µg\ml	[4]
2.	Allopurinol	In tablets	Reagents: Catechol and ammonium ferrous sulphate Wavelength: 580 nm Solvent: 0.1M KOH Linearity range:2-10 µg\ml	[5]
3.	Allopurinol	Bulk and pharmaceutical dosage form	Wavelength: Method A – 250 nm Method B – 238 nm Method C – 245-255 nm Solvent: Methanol, Water Linearity range:5–35 µg\ml	[6]
4.	Allopurinol And α-Lipoic acid	In combined dosage form	Wavelength: Allopurinol – 250 nm α-Lipoic acid- 380 nm Solvent: Methanol Linearity range: Allopurinol: 10-50 µg\ml α-Lipoic acid: 10-50 µg\ml	[3]
5.	Febuxostat And Allopurinol	In synthetic mixture	Wavelength: Isoadsorptive point-274 nm Allopurinol -250 nm Solvent: Methanol	[7]

			Linearity range: Febuxostat:2-12 µg\ml Allopurinol:2-12 µg\ml	
6.	**Allopurinol**	**In tablet dosage form**	**Wavelength:250nm Solvent: 0.1N NaOH Linearity range: 5-25 µg\ml**	**[8]**
7.	**Allopurinol and Benzbromarone**	**In bulk powder and combined dosage form**	**Solvents: Methanol Wavelengths: Method-1: 225-275nm Method-2: 250-238 nm Method-3: 245-257nm Method-4: 243.6 nm Method-5: 243.6 nm**	**[9]**

Table 2: Methods for estimation of Allopurinol single and combination with other drugs by UPLC

8.	**Allopurinol**	**In pharmaceutical preparation**	**Detection wavelength: 254 nm Mobile phase: 0.05m monobasic AmmoniumSulphate (Ammonium Dihydrogen Phosphate) Column: Chromosil C_{18} Flow rate: 0.55 ml\min Range:50-150% Retention time: 0.9min**	**[10]**
9.	**Allopurinol**	**In pharmaceutical dosage form**	**Detectionwavelength: 220 nm Mobile phase:sodium perchlorate (10 mM, pH 3.0)and acetonitrile gradient programme (TminA:B) T0100:00, T4100:00, T1430:70 with a post-run time of 2.5 min. Column: Waters Acquity UPLC HSS T3P column Flow rate: 0.5 ml\min Range:50-150% Retention time: Allopurinol – 4.2 mins Imp-1 – 1.202 mins Imp-2 – 2.945 mins Imp-3 – 3.159 mins Imp-4 – 8.123 mins Imp-5 - 8.312 mins**	**[11]**

Table 3: Methods for estimation of Allopurinol single and combination with other drugs by LC-TMS

10.	**Allopurinol and Oxypurinol**	**In human plasma and urine**	**Mobile phase: Methanol and ammonium formate–formic acid buffer containing 5 mM ammonium formate and0.1% formic acid (95:5, v/v) as the mobile phase (A) for allopurinol or methanol plus 5 mM ammoniumformate aqueous solution (95:5, v/v) as the mobile phase (B) for oxypurinol Column: Agilent Eclipse Plus C_{18} Flow rate: 0.5ml\min Linearity range: Allopurinol: 0.5-30 µg\ml Oxypurinol: 1-50 µg\ml Retention time: Allopurinol: 7 mins Oxypurinol: 4 mins**	**[12]**
			Mobile phase: 0.1% (v/v) FA in water-ACN (98:2, v/v). For isocraticelutionthe flow rate of the mobile phase was split in 70:30 (v/v) ratio Column: Hypersil Gold Flow rate: 0.5 ml\min Linearity range:	

11.	**Allopurinol and Oxypurinol**	**In human plasma**	**Allopurinol: 500–5000 ng\ml Oxypurinol:400–20,000ng\ml Retention time: HPLC-UV: Allopurinol: 4.58 mins Oxypurinol: 12.3 mins LC-MS/MS: Allopurinol: 5.85 mins Oxypurinol: 2.57 mins**	**[13]**
12.	**Allopurinol, Oxypurinol & Lesinurad**	**In plasma**	**Mobile phase: Acetonitrile, water and formic acid (95:5:0.1, v/v/v) Column: Acquity UPLC HILIC Flow rate: 0.3 ml\min Linearity range: Allopurinol: 22–8000 ng/mL Oxypurinol:33–12000 ng/mL Lesinurad: 25–9000 ng/mL Retention time:0.3 ml/min**	**[14]**

Table 4: Methods for estimation of Allopurinol single and combination with other drugs by HPLC

13.	**Allopurinol and Oxypurinol**	**?**	**Detection wavelength: 254 nm Mobile phase: Sodium acetate (0.02 M; pH 4.5) Column: LiChrospher 100 RP-18 Flow rate: 1ml\min Linearity range: Allopurinol: 0.5–10 mg/L Oxypurinol: 1–40 mg/L Retention time: Allopurinol: 12.3 min Oxypurinol: 9.9 min**	**[15]**
14.	**Allopurinol, Benzbromarone & Oxypurinol**	**In active metabolite**	**Detectionwavelength: 250 nm Mobile phase:0.01 Mphosphate buffer pH: 4.0- acetonitrile-methanol (50:30: 20 v/v/v) Column: Agilent C_{18} Flow rate: 1.0 ml\min Linearity range: 1-10 ug/ml Retention time: Allopurinol: 4.05 mins Benzbromarone: 6.48 Oxypurinol:2.56 mins**	**[16]**
15.	**Allopurinol and Oxypurinol**	**In plasma**	**Detection wavelength: 280 nm Mobile phase: Phosphoric acid aqueous solution（pH-1.8） Column: Cosmosil C_{18} Flow rate: 1.0 ml\min Retention time: Allopurinol: 13.5 min Oxypurinol: 11.9 min**	**[17]**
16.	**Allopurinol and Benzbromarone**	**In combined dosage form**	**Detectionwavelength: 260 nm Mobile phase: Sodium acetate: Acetonitrile: Triethylamine (50:50:0.5) Column:ZorbaxC_{18} Flow rate: 1 ml\min Linearity range: Allopurinol:3- 50µg/mL^{-1} Benzbromarone: 3- 50µg/mL^{-1} Retention time: Allopurinol: 4.3 mins Benzbromarone: 1.26 mins**	**[18]**

17.	**Allopurinol and α-lipoic acid**	**In tablets**	**Detectionwavelength: 210 nm Mobile phase: acetonitrile: 0.02M ammonium acetate buffer adjusted to pH 4.650:50 v\v Column: Enable C_{18}G Flow rate: 0.8 ml\min Linearity range: 50-175µg\ml Retention time: Allopurinol: 3.01 mins α-lipoic acid: 8.42 mins**	**[19]**
18.	**Allopurinol and α-lipoic acid**	**Bulk drug and tablet dosage form**	**Detectionwavelength: 230 nm Mobile phase: Tetrabutylammoniumhydroxide buffer and acetonitrile(70:30v/v) Adjusted to pH 6.6 Column: Inertsil ODS C_{18} Flow rate: 0.8 ml\min Linearity range: 250-750 µg\ml Retention time: Allopurinol: 2.33 mins α-lipoic acid: 6.32 mins**	**[20]**
19.	**Allopurinol**	**In Tablets**	**Detectionwavelength: 254 nm Mobile phase: 0.05 M Potassium dihydrogen phosphate Column: Hypersil ODS, C18 Flow rate: 1.5 ml\min Linearity range: 0.051–0.760 µg/mL Retention time: Allopurinol: 10 mins IMP-A: 3.516 mins IMP-B: 7.428 mins**	**[21]**
20.	**Lesinurad and Allopurinol**	**API & marketed formulation**	**Detectionwavelength: 255 nm Mobile phase: phosphate buffer: methanol 55:45% v/v Column: Zorbax C_{18} Flow rate: 1 ml\min Linearity range: 1-5 µg\ml Retention time: Lesinurad: 2.061 mins Allopurinol: 2.462 mins**	**[22]**
21.	**Lesinurad and Allopurinol**	**API**	**Detection Wavelength: 250 nm Mobile phase:Acetonitrile: Methanol: 0.1% Triethylamine buffer (pH-adjusted to 3 usingorthophosphoricacid) 25:35:40 (v/v/v). Column: Inertsil C_{18} Flow rate: 1 ml\min Linearity range: 5-25µg\ml Retention time: Allopurinol: 2.60 mins Lesinurad: 5.57 mins**	**[23]**
22.	**Lesinurad and Allopurinol**	**API and Pharmaceutical dosage form**	**Detection wavelength: 255 nm Mobile phase: 0.1% trifluoroacetic acid and methanol in the ratio of 40:60 v/v Column: InertsilODS C_{18} Flow rate: 1 ml\min Retention time: Allopurinol: 2.4 mins Lesinurad: 3.3 mins**	**[24]**

23.	**Allopurinol**	**In serum**	**Detectionwavelength: 242 nm Mobile phase: Sodium acetate: trichloro acetic acid: water Column: ZORBAX, SB C_{18} Flow rate: 1.0 ml\min Linearity range: 0.5-12.5 µg/ml Retention time: 1.6 mins**	**[25]**
24.	**Allopurinol and Lesinurad**	**Raw and tablet form**	**Detectionwavelength: 239 nm Mobile phase: Methanol: acetonitrile:0.05 M phosphate buffer, pH 6.2 (25:60:15 v/v/v) Column: Hypersorb ODS C18 Flow rate: 1 ml\min Linearity range: Allopurinol:0.022 µg/ml Lesinurad: 0.067 µg/ml,**	**[1]**

CONCLUSION

A broad range of techniques is available in the estimation of Allopurinol in bulk drug and different pharmaceutical dosage forms. From the analysis of documented data out of all these techniques HPLC with UV detection was extensively used with mobile phases Methanol, Acetonitrile and Acetate and phosphate buffer with a flow rate of 0.8-1.5 ml\min and retention time <15 min because this approach offers reliable and low cost in comparison with more advanced technology. This review was carried out on the summary of the current state of the art of analytical methods for the determination of Allopurinol.

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