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Mini Review

Analytical Methods for the Determination of Anti-Gout Drugs

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Abstract

Gout is a type of arthritis in which small crystals form inside and around the joints. It causes sudden attacks of severe pain and swelling. Different classes of drugs are used for both acute and chronic gout disease. The present review has clearly covers the analytical methods developed for the estimation of anti-gout drugs in the literature. This review helps the authors to propose new methods after a thorough verification of the advantages and the disadvantages of the established methods.

Keywords: RRLC; RP-HPLC; Spectrophotometry; LC-MS; TLC; HPTLC

Introduction

Gout is the common form of inflammatory arthritis. When there is an excess urination in the body it crystalizes in joint fluid, cartilage, bones, tendons or other sites. These crystals can directly cause an acute inflammatory attack [1]. This disease results from the deposition of monosodium uric crystals in the tissues. It is a systemic disease which increases the serum uric acid. These monosodium urate crystals can be deposited in all the tissues mainly in joints. It is an acute inflammation that can quickly relive by the non steroidal anti-inflammatory drugs (NSAIDS) [2-5]. Gout is very painful form of arthritis and is seen mainly in men over 50 years of age. Now-a-days it is also seen in the women and children it causes because of people consuming excess of fats which contribute heavily for the formation of purine break down and the uric acid. Gout is a metabolic disorder caused by high body uric acid levels and it is marked by the episodic deposition of uric acid crystals in joints and other tissues such as kidney. The disease of gout can be cured with medicinal herbs without any side effects.

The gout can categorised into two types: 1) Acute gout. 2) Chronic gout. Acute gout is a painful inflammation causes one or few joints. Mainly there are 3 stages for the management of gout -by treating acute attack, by lowering excess stores of the uric acid to prevent flares of gout arthritis and tissue deposition and by preventing acute flares and drugs used in the treatment of acute gout are classified as Colchicine, NSAIDS (Diclofenac, Naproxen, Ibuprofen, Indomethacin) and Steroids. Chronic gout is a destructive arthritis and causes repeated pain and inflammation and drugs used in the treatment of chronic gout are classified as Uric acid synthesis inhibitors (Allopurinol, Febuxostat) and Inhibit tubular reabsorption of uric acid (Probenecid, Sulfinpyrazone) [6,7]. The chemical structures of these drugs were shown in Figure 1.

Analytical method development includes different instruments and no one can confirm the suitability of the method particularly when a category/class of drugs are chosen. It's not possible to propose a single method for the entire class of drugs as it depends on the physio chemical characteristics and the compatibility of the instruments and columns used especially in case of chromatographic techniques. Therefore the authors reviewed the literature to compile the analytical methods so far developed for this class of drugs.

History

Colchicine is an alkaloid derivative and chemically N-[(7S)1,2,3,10-tetramethoxy-9-oxo-5,6,7,9tetrahydrobenzo[a] heptalen-7-yl] acetamide) and acts by inhibiting the inflammation process and control the gout inflammation and pain. Diclofenac is an antipyretic drug and chemically Sodium 2-(2,6-dichlorophenyl-aminophenyl acetate. It is a NSAIDs acts by inhibiting COX and PG synthesis. Allopurinol is chemically 1H, 2H, 4H-pyrazolo [3, 4-d] pyrimidin-4-one and acts by inhibiting xanthine oxidase. Febuxostat is chemically 2-[3-cyano4-(2-methylpropoxy) phenyl]-4-methyl-1, 3 thiazole-5-carboxylic acid and acts by inhibiting xanthine oxidase enzyme. Probenecid is chemically 4-(dipropyl sulfamoyl) benzoic acid and acts by inhibiting the renal excretion of the organic anions and reduce tubular reabsorption. In the present review the authors have assembled the analytical methods established so far in the literature for the determination of the above listed anti-gout drugs.

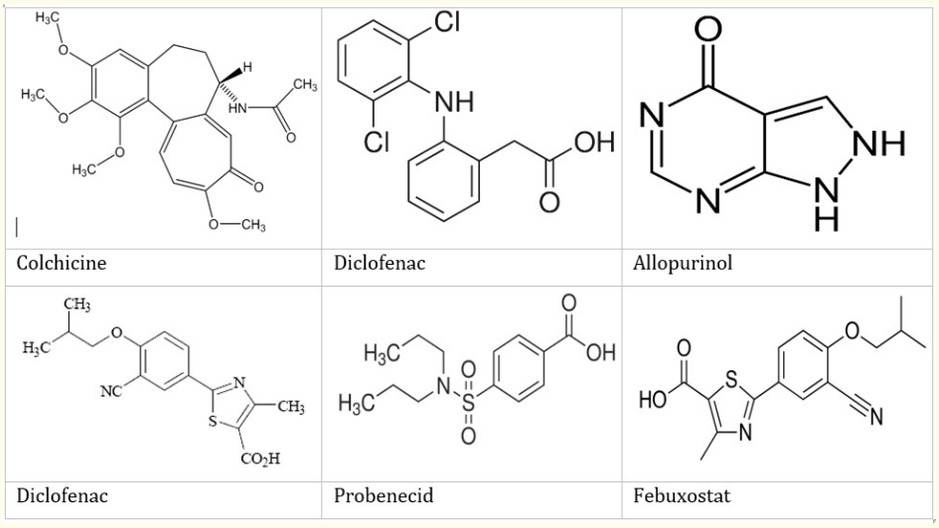

Figure 1: Chemical structures of drugs used for the treatment of gout disease.

Analytical methods

Anti-gout drugs were quantified using different analytical techniques. Sukhdev et al developed the rapid resolution liquid chromatography [8] for Allopurinol and its degradation products and many RP-HPLC methods [9-29], Spectrophotometry [30-44], TLC [45], HPTLC [46,47], LC-MS/MS [48] and LC-MS [49] techniques were established for the determination of anti-gout drugs. A brief description of the analytical methods so far developed were summarized in Table 1 for RP-HPLC methods, Table 2 for Spectrophotometry, Table 3 for TLC and HPTLC and Table 4 for the mass spectrometric methods. Te available brands and formulations in India were incorporated in Table 5.

Drug	Column	Mobile phase (v/v) / Detection wavelength (nm)	Flow rate (mL/min)	Comment	Ref
Allopurinol	Zorbax SB C8 (1.8 µm, 4.6 X 50 mm)	Potassium dihydrogen phosphate buffer (pH 2.5) (0.025M) : Methanol / 230	1.0	RP-RRLC Fast elution and buffers are used	8
Allopurinol and Alpha lipoic acid	C18 column (250 × 4.6 mm; 5 µ)	Tetra butyl ammonium hydroxide buffer: Acetonitrile (70:30) / 230	0.8	HPLC Fast elution and buffers are used	9
Allopurinol and Alpha lipoic acid	C18G (250 X 4.6 mm; 5µ)	Acetonitrile: 0.02M Ammonium acetate buffer (50:50) / 230	0.8	HPLC Fast elution and buffers are used	10
Allopurinol and Oxypurinol	Lichrocart® 125-4 Lichrospher ® 100 RP-8 (5µm)	0.1% Water, 88% Formic acid and 0.25% Acetonitrile/ 254	0.7	HPLC Fast elution and buffers are used	11
Colchicine	C18 (250 x 4 mm, 5µ)	Acetonitrile, Methanol, Water, 0.1% OPA (50:30:15:5)/ 257	1.0	HPLC Fast elution	12
Colchicine	C18 (250 x 4.6 mm, 5µm)	Acetonitrile : Methanol : Water (32:48:20)/ 254	1.2	HPLC Fast elution	13
Colchicine	Inertsil ODS-2, 5 mm, 250 ×4 mm	0.05M Ammonium acetate: Methanol (48:52)/ 245	1	HPLC Fast elution and buffers are used	14

Colchicine	Zorbax RX C8 (250 x 4.6 mm, 5 µm)	Buffer (pH 5.2) and Methanol (62:38)/ 254	1	HPLC Fast elution and buffers are used	15
Colchicine	5 mm C18 column (Luna, Phenomenex, Torrance, CA)	Acetonitrile; Monosodium phosphate (pH 3.0) (35:65)/245	1	HPLC Fast elution and buffers are used	16
Diclofenac	C18 (4.6 ×150 mm, 3µm)	0.05M Orthophosphoric (pH 2): Acetonitrile(35:65)/ 210	2	HPLC Fast elution and buffers are used	17
Diclofenac Sodium and Chlorzoxazone	ACE 5 C18 column (150 ×4.6 mm;5µm	Orthophosphoric acid: Acetonitrile: Methanol (30: 30: 40)/ 279	1	HPLC Fast elution and buffers are used	18
Diclofenac Sodium and Drotaverine Hydrochloride	C8	Acetonitrile(0.02M): Ammonium acetate buffer (53:47)/ 230	1	HPLC Fast elution and buffers are used	19
Diclofenac Sodium and Diflunisal	Zorbax SB-C8 (250 x 4.6mm, 5 µm)	0.05 M Phosphoric acid: Acetonitrile: Methanol (40:48:12)/ 228	1	HPLC Fast elution and buffers are used	20
Diclofenac Sodium and Lidocaine Hydrochloride	C18 (150 x 3.9 mm, 5 µm)	0.05 M Orthophosphoric acid: Acetonitrile/ 220	1.5	HPLC Fast elution and buffers are used	21
Diclofenac Potassium	ODS/ Cyano; ACE (100 x 4.6 mm, 5 µm)	Methanol: Potassium dihydrogen phosphate buffer (50 : 50)/ 280	1.5	HPLC Fast elution and buffers are used	22
Febuxostat	Nucleosil C18 (250 x 4.6 mm, 5µm)	0.2% Triethyl amine: Acetonitrile (15: 85)/ 275	1.2	HPLC Fast elution and buffers are used	23
Febuxostat	C18 (250 x 4.6 mm, 5µm)	Phosphate buffer (pH 2.5) : Methanol(20:80)/ 315	1	HPLC Fast elution and buffers are used	24
Febuxostat	Zodiac C18 (250 × 4.6 mm, 5µ)	Acetonitrile : Methanol (85:15)/ 218	1.1	HPLC Fast elution	25
Febuxostat and Ketorolac	C18 (150 × 4.6 mm, 5µ)	Tri ethyl amine buffer: Acetonitrile (60:40)/ 255	1	HPLC Fast elution and buffers are used	26
Probenecid and Amoxycillin trihydrate	Zorbax RX-C18 (150 × 4.6 mm, 5µ)	Mixture of 0.05M KH_2PO_4 buffer (pH 5.6) adjusted with TFA + THF 0.5%: Acetonitrile (86:14)/ 227	0.8	HPLC Fast elution and buffers are used	27
Probenecid and Cefadroxil	Princeton SPHER-100 C18 (250 x 4.6 mm, 5µ)	Acetonitrile: Phosphate buffer (pH 2.5) (60:40)/ 242	1	HPLC Fast elution and buffers are used	28
Probenecid and Cefadroxil	C18 (250 x 4.6 mm, 5µ)	Orthophosphoric acid: Acetonitrile (20:80)/ 226	1	HPLC Fast elution and buffers are used	29

Table 1: List of liquid chromatographic methods for the assay of Anti-Gout Drugs.

Drug	Method	Reagent	λ (nm)	Linearity (µg/mL)	Ref
Allopurinol	UV	Distilled water	250.5	1-20	30
Allopurinol	UV	Phosphate buffer (pH 6.8)	250	4-14	31
Allopurinol and α-lipoic acid	UV	methanol	250	10-50	32
Allopurinol And Benzbromarone	UV	methanol	233 253	2-16 1-16	33
Colchicine	UV	Phosphate buffer saline (pH 6.4)	353.8	6-22	34
Febuxostat	UV	Methanol	315	0.2-15	35
Febuxostat	UV	Phosphate buffer (pH 6.8)	312	1-10	36
Febuxostat	UV	Methonal	316	2-20	37
Febuxostat	UV	Methonal	315	2-10	38
Febuxostat	UV	0.1N NaOH	314	1-6	39
Febuxostat and Allopurinol	UV	Phosphate buffer (pH 6)	314	2-30	40
Probenecid	UV	phosphate buffer (pH 6.8)	243	0-40	41
Probenecid	UV	2M Sodium acetate	244.5	2-26	42
Probenecid and Amoxicillin	UV	Methanol	233	5-20	43
Probenecid and Cefadroxil	UV	0.1N HCl	237.8 260	2-25 4-36	44

Table 2: List of spectrophotometric methods for the assay of Anti-Gout Drugs.

Drug	Method	Mobile phase	λ (nm)	Ref
Colchicine and Probenecid	TLC	Toluene: Ethyl acetate: Methanol: Ammonia (30:20:20:0.1 v/v/v/v)	248	45
Colchicine	HPTLC	Methylene chloride: Methanol (95:5 v/v)	245	46
Febuxostat and Diclofenac	HPTLC	Chloroform: Methanol (7:3 v/v)	289	47

Table 3: List of thin layer chromatographic methods for the assay of Anti-Gout Drugs.

Drug	Method	Column	Mobile phase	Flow rate (mL/min)	λ (nm)	Ref
Allopurinol	LCMS	Symmetry Shield, RP8, 3.5µm, 4.6 x 100 mm	Ammonium acetate: Methanol (80:20v/v)	0.6	245-255	48
Allopurinol and Oxypurinol	LCMS	Hypersil Gold (150 mm × 4.6 mm, 5 µm) column	0.1 % Formic acid: Acetonitrile (98:2 v/v)	0.5		49

Table 4: List of LC-MS methods for the assay of Anti-Gout Drugs.

Drug	Dosage forms	Brand names	LabelClaim (mg)	Pharmaceutical company
Allopurinol	Tablet	Allgoric	100	Kamron
	EXT-TAB	Aligout	10	Biomax
	Tablet	Aloriv	100	East African
	Tablet	Ambilast	100	Aamorb (St.Morison)
	Tablet	Biorinol	100	Biochemix
	Tablet	Burin	100	Pharmacon
	Tablet	Gudloric	100	Candor
	Tablet	Gurik	100	Zee Lab
	SR-CAP	Logout -SR	250	Inga
	Tablet	Louric	100	Olcare
	Tablet	Satric	100	Zytras
	Tablet	Soviric	100	Gopal (Sovia)
	Tablet	Swiloric	100	Ind-Swift
	Tablet	Z -Nol	100	Arlak Biotech
	Dispertab	Zytol	100	Novaduo Pharma
Allopurinol and Alpha lipoic acid	Tablet	Aluno	100 A:100 L	Salud care
Colchicine	Tablet	Colchicindon	0.5	Zydus (Alidac)
	Tablet	Coljoy	5.0	Cadila (Vibra)
	Tablet	Goutnil	0.5	Inga
	Tablet	Zycolchin	0.5	Zydus (Synovia)
Diclofenac	Tablets	3-D	11.6	Intas
	Injection AMP	Aclomax	-	Admac
	AMP	Acnec	25	Acme
	Injection	Ack Ack	75 mg/3 ml	Unique
	GEL	Adgel	A 1%	Adly
	Injection	Adic -K	25 mg in 1 ml	Ultra-Drugs
	Gel	Adiflam	1% w/w	Leben Labs
	Tablet	Agile -K	50	Ind-Swift
	Injection	Agile	75 mg/3 ml	Ind -Swift
	Injection	Alcidic	25	Alcure Pharma
	Injection	Alefen	25 mg/ml	Allenge
	GEL	Arthin	30 g	Allegene
	Tablet	Artilov	50	Uniorange
Diclofenac Sodium and Diflunisal	Tablet	Dersy	100	Worth Medicines
	Injection	Dicax	75 mg/3 ml	Axyzen
	Injection	Diclam	-	Amrit Remedies
Febuxostat	Tablet	Alxo	40	Alpic biotech
	Tablet	Exfeb	40	Olcare
	Tablet	Feboage	40	Allenge
	Tablet	Lofu	40	Olcare
	Tablet	Zurig	80	Cadila HC

Table 5: List of available marketed formulations of Anti-Gout Drugs.

Conclusions

This review article will be very helpful for the authors to compare any new analytical method developed in the world of analytical chemistry for the determination of Anti-Gout drugs.

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