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Review Article

Spectroscopic, Chromatographic and Electrochemical Determination of Indomethacin in Different Matrices

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Abstract. In this literature review, we will introduce most of up-to-date reported methods that have been developed for determination of an important Nonsteroidal Anti-Inflammatory Drug (NSAID) which is indomethacin in its pure form, combined form with other drugs, combined form with degradation products, and in biological samples.

Keywords: literature review; NSAID; indomethacin, degradation products, biological samples

Introduction

Indomethacin (IDM) [1-(4-chloro benzoyl)-5-methoxy-2-methyl-indol-3-yllacetic acid] is an indole derivative as seen in Figure 1. It has analgesic, anti-inflammatory and antipyretic action and also used in case of rheumatoid arthritis. The common side effects are GIT ulceration and bleeding, headache, depression, drowsiness, tinnitus, confusion, lightheadedness, insomnia, dizziness, convulsions, coma, hypertension and blood disorders (Sastry, Mangala, & Rao, 1986).

Many analytical techniques have been used for the determination of IDM in different forms. As such, in this review article, IDM has been studied in respect of chemical characters, mode of action and most reported analytical methods that have been developed for determination of this drug in different matrices.

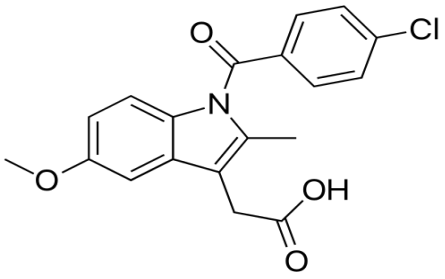

Figure 1: Chemical structure of IDM

Pharmacological Action

IDM has potent inhibitory effect on the synthesis of prostaglandins. The production of prostaglandins is inhibited through the inhibition of (COX) 1 and 2 and is essential for most of the non-steroidal anti-inflammatory drugs (NSAIDs). The indications for NSAIDs, and in particular IDM, include arthritis, fever, various headache syndromes, and dysmenorrheal (Summ & Evers, 2013).

Review of Analytical Methods

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Various techniques were used for the analysis of IDM in its pure forms, in pharmaceutical formulations and in biological fluids. The available reported methods in the literature can be summarized as follows:

Spectroscopic Methods

Spectrophotometric Methods

Drugs	Matrix	Method or reagent	λ_{max}(nm)	Linearity range	LOD	Ref.
IDM	Capsules	Coloremetric spectrophotometry by using mAP - CAT reagent	490	4-16 µg/mL	------	Sastry, Mangala, and Rao(1986)
IDM	Capsules	Partial least square method	578	0.05-4.0 mg/10 mL	0.05 mg/10 mL	Noreen et al. (2007)
IDM	Capsules	N –bromosuccinimide reagent	227	0.02-0.16 mg /10 ml	------	Hassib, Safwat, and El-Bagry (1986)
IDM	Capsules	4-carboxyl-2,6-dinitrobenzene diazonium ion reagent	470	3–11 µg/mL	0.90 µg/mL	Adegoke, Idowu, and Olaniyi (2006)
IDM	Capsules	UV spectroscopy	228	1-10 mg/L	0.602-0.129 mg/L	Ali, Albakaa, and Ali (2015)
IDM and ketoprofen	Capsules	Diphenylamine sulfonate (DPAS) redox indicator	250	0.72-14.31 µg/mL	0.27 µg/mL	Zayed and Farouk (2017)
IDM	Capsules	UV Spectroscopic method	266	1-6 µg/mL	0.17273 µg/mL	Thejomoorthy et al. (2019)
IDM	Biological fluids	Surfactant coated magnetic nanoparticle-based solid-phase-extraction-coupled-withspectrophotometric detection	310	25-450 ng/mL	8.6 ng/mL	Amoli-Diva, Pourghazi, and Pourasadollah-Karani (2015)
IDM	Capsules	Diazotized p-phenylenediamine dihydro chloride (PPDD) in sulphuric acid medium	510	0.2-10 µg/mL	0.16 µg/mL	Nagaraja, Vasantha, and Yathirajan (2003)
IDM	Capsule, tablets and suppositories	2-Nitrophenylhydrazine hydrochloride	552	0.4-2 µmole/10 mL	------	Abdel-hay et al. (1990)
IDM, Alfuzocin, esomprazole, andketorolac	Capsules and tablets	Oxidation by using alkaline $KMnO_4$	610	2.5-15 µgm/L	0.21 µg/mL	Reddy, Sayanna, and Venkateshwarlu (2014)
IDM,diclofenac sodium, ibuprofen, ketoprofen, ketorolac tromethamine, mefenamic acid, and naproxen	Capsules	Extractive-spectrophotometric determination using methylene blue	654	0.04–8.5 µg/mL	0.01 µg/mL	El-Kommos, Mohamed, and Abdel Hakiem (2013)

SpectrofluorometricMethods

Drugs	Matrix	Fluorogenic reagent (method)	λ_{ex} (nm)	λ_{em} (nm)	Linearity range	LOD	Ref.
IDM	Capsules	mAP - CAT reagent	465	490	0.2-3 µg/mL	------	Sastry, Mangala, & Rao (1986)
IDM	Capsules	alkaline hydrolysis in micellar medium	278	358	up to 10^{-5}mol/L	1.6×10^{-8}mol/L	Pinto et al. (2005)
IDM	Capsules	Potassium hexacyanoferrate (III)	226	------	0.01- 5 mmol/L	320.222 ng/sample	Turkie, &Abd-Alrazack (2009)

Chromatographic Methods

HPLC Methods

Drugs	Matrix	Column	Mobile phase	Detector	Linearity range	LOD	Ref
IDM	Plasma	Hypersil ODS C_{18} column (5 µm, 125 mm × 4 mm)	Methanol, water and orthophosphoric acid (70:29.5:0.5, v/v/v)	UV at 270 nm	25-2500 µg/L	5 µg/L	Al Za'abi et al. (2006)
IDM	Plasma	Phenomenex C_{18} (5 µm, 150 mm × 4.6 mm)	63% acetonitrile and 37% water (pH2.0, adjusted with 0.2% ortho phosphoric acid)	UV at 270 nm	10-200 ng/mL	3 ng/mL	Dawidowicz, Kondziola, and Kobielski (2009)
IDM and mefenamic acid	Plasma	Vydac C_{18} (5 µm, 250 mm × 4.6 mm)	10 mM phosphoric acid-acetonitrile (40:60, v/v)	UV at 280 nm	0.1-10 µg/mL	0.06 µg /mL	Niopas and Mamzoridi (1994)
IDM and its two degradant impurities 4-chlorobenzoic acid, 5-methoxy-2-methyl-indoleacetic acid	Capsules	Zorbax Eclipse Plus C_{18} (3.5 µm, 100 mm × 4.6 mm)	Methanol: acetonitrile: 10 mM sodium acetate buffer pH 3, 10:50:40% v/v	UV at 254 nm	25-70 µg/mL	1.036 µg/mL	Pai and Sawant (2017)
IDM	Plasma	LiChrosorb-RP_{18} (7 µm, 250 mm × 4 mm)	6 mM Phosphoric acid–acetonitrile (50:50)	UV at 205 nm	0.1–2.0 µg/mL	0.05 µg/mL	Sato et al. (1997)
IDM and acemetacin	Urine	Promosil C_{18} (5 µm, 250 mm × 4.6 mm)	Water : acetonitrile (43:57, v/v, containing 0.5‰ trifluoroacetic acid)	UV at 254 nm	0.1–50 µg/mL	0.027 µg/mL	Yuan et al. (2016)
IDM desmethylindomethacin, deschlorobenzoylindomethacin and desmethyldeschlorobenzoylindometbacin	Plasma	Whatman C_{18} (10 µm, 250 mm × 4.6 mm)	22.5% or 26% acetonitrile in 25% acetic acid.	Fluorometric detection at 390 nm	25-200 ng/mL	25 ng/mL	Bernstein and Evans (1982)
IDM	Rat plasma	Zorbax Eclipse XDB C_{18}	Methanol:0.1% phosphoric acid (70:30, v/v)	UV at 254 nm	50-10000 ng/mL	10 ng/mL	Liu et al. (2002)
IDM	Serum	Stainless-steel column (150 mm x 4.6 mm I.D.) packed with Unisil Q C_{l8} (5 um)	0.07 M phosphate buffer (pH 6.6)-acetonitrile (65 : 35 v/v) containing 180 mM hydrogen peroxide	Fluorometric detection at 462 nm	0.05-30 µg/mL	10 ng/mL	Mawatari, Iinuma, and Watanabe (1989)
IDM	Urine	Nucleosil RP-C_{18} (5 µm, 250 mm × 4.6 mm)	Methanol:water:acetic acid = 67:33:0.1	Flow injection chemiluminescence (CL) detection	0.01-10 µg/mL	8 ng/mL	Zhang et al. (2007)
IDM	Porcine plasma	Res Elut RP C_{18} (5 µm, 150 mm × 4.6 mm)	60% acetonitrile in 0.02M sodium acetate buffer adjusted to pH 3.6 using orthophosphoric acid	UV at 320 nm	50–3000 ng/mL	10 ng/mL	Boon, Glass, and Nimmo (2006)
IDM	Serum	C_{18}-bonded vinyl alcohol copolymer column	pH 10.0, 35% acetonitrile in phosphate buffer	Fluorimetric detection at 375 nm	0.1-10.0 µg/mL	10 ng/mL	Kubo et al. (1992)

IDM	Serum	Inertsil ODS-2 (5 µm, 150 mm × 4.6 mm)	pH 7.0, 35% acetonitrile in phosphate buffer containing hydrogen peroxide as a fluorogenic reagent	Fluorimetric detection at 462 nm	2.5-15.0 µg/mL	0.5 µg/mL	Kubo et al. (1993)
IDM	Residues in poultry	Spherisorb ODS-2 column (200 mm×3.9 mm, 5 µm)	Acetonitrile–acetic acid (0.5% in water) (50:50).	UV at 254 nm	20–500 ng/g	20 ng/g	Cristofol et al. (1998)
IDM, diclofenac sodium and phenylbutazone	Urine	Waters Nova-Pack C_{18} (15 cm×3.9 mm, 4 µm)	10 mMacetate buffer (pH 4.0)–acetonitrile (58:42, v/v)	UV at 210 nm	0.02–1.0 µg/mL	0.007 µg/mL	Bakkali et al. (1999)
Methotrexate and IDM	Urine	Octylsilica	Acetate buffer (pH 4; 10 mM)–methanol (60:40, v/v)	UV at 400 nm	0.1-8 µg/mL	0.01 µg/mL	Michail and Moneeb (2011)
IDM	Suppositories	C_{18}	0.05 mol·L-1 acetic acid-acetonnitrile (50:50)	UV at 260 nm	25.59-307.13 mg/L	---- ----	Zheng and Chen (2012)
Diclophenacsodium,flufenamic acid, IDM, ketoprofen	Capsules	Shim-pack GLC-CN, 5 µm, (150×4 mm)	Acetonitrile and 20 mM ammonium acetate solution (5:1 v/v)	APCI-MS, m/z 355.8	100-500 ng/mL	4.0 ng/mL	Abdel-Hamid, Novotny, and Hamza (2001)
IDM	Maternal plasma and urine	Waters Symmetry C_{18} column (150 mm × 4.6 mm, 5 µm)	0.05% (v/v) formic acid aqueous solution and acetonitrile (47:53, v/v)	MS/MS, m/z 139	14.8-2.97 $\times10^3$ng/mL for plasma &10.5-4.21 $\times10^3$ng/mL for urine	3.71 ng/mL &2.63 ng/mL	Wang et al. (2013)
IDM	Aqueous media	Gemini C_{18} (5 m, 250 mm × 4.6 mm)	Water with 1% formic acid (A) and acetonitrile	MS	1×10^{-4}- 1×10^{-6}M	------	Temussi et al. (2011)
IDM	Plasma & uterine tissue	Diamonsil C $_{18}$ (150 × 4.6 mm, 5 µ m)	Methanol, acetonitrile, water and formic acid (45:45:10:0.5, v/v/v/v)	MS/MS, m/z 358→111	2.0–400 ng/mL for plasma &4.0–800 ng/mL for uterine tissue	0.6 ng/mL	Liu et al. (2012)
IDM	Aliquots of vitreous humor, aqueous humor	Gemini-NX C_{18} (2.0 x 50 mm, 3 mm)	Water/acetonitrile (50:50, vol/vol).	MS/MS	1-1000 ng/mL	0.33 ng/mL	Bucolo et al. (2011)
IDM	blood and buccal smear samples	Waters SymmetryC_{18} (2.1 mm × 100 mm, 3.5 µm)	Acetonitrile with 0.05% formic acid (v/v) and (B) 0.05% formic acid aqueous solution (v/v);	MS/MS	6.22 - 1.59 $\times 10^3$ ng/mL	2.073 ng/mL	Shah et al. (2019)
IDM	Human liver	InertsilPh C_{18} (4.6 × 150 mm)	1% formic acid-acetonitrile (6:4, v/v)	MS	0.2–20 µM	------	Mano, Usui, and Kamimura (2007)
IDM, paracetamol and 1-naphthol	Human intestinal cell line	Waters XBridge Shield RP_{18} (2.1 mm × 50 mm, 3.5 µm)	2 mM ammonium acetate (A, pH 7.0) and acetonitrile	MS/MS	5-500 µM	------	Siissalo et al. (2010)
IDM	Cunninghamellablakesleeana	Diamonsil C_{18} (200×4.0 mm, 5 µm)	Acetonitrile-water-formic acid (70:30:0.5, v:v:v)	UV at 230 nm	------	16.6 ng/mL	Zhang et al. (2006)
IDM	Topical gel	Zorbax SB-CN (150 mm × 4.6 mm, 5 µm)	Acetonitrile and 0.2% phosphoric acid (50:50, v/v)	UV at 237 nm	100–500 mg/L	10 ng/L	Nováková et al. (2005)

Electrochemical Methods

Drug	Matrix	Electrode	Linearity range	L.O.D	REF
IDM	Tablets and capsules	GNRs–GO–CNTP/GCE	0.2–0.9 and 2.5–91.5 µM	1.7 × 10^{-2}µM	Arvand and Gholizadeh (2013)
Diclofenac and IDM	Tablets	MWCNT–IL/CCE	1–50 mol/L	0.26 mol/L	Sarhangzadeh et al. (2013)
Mefenamic acid and IND	Tablets	MWCNTs-Fe (III)-schiff base	0.08–435 mol/L	0.08 mol/L	Hasanzadeh et al. (2012)
IDM and mefenamic acid	Tablets	(P(CS)-CuNP-CuE)	0.001 -5000 µM	1 nM	Farshchi et al. (2020)
IDM	Tablets	Carbon paste electrodes	8.5 × 10^{-8} - 1.5 × 10^{-7} M	2.5 × 10^{-8} M	Radi (1998)
IDM	Tablets	Ion-selective electrodes (ISE)	1×10−4 - 5×10^{-2}mol/L	3×10^{-5}mol/L	Kormosh, Hunka, and Bazel (2009)
IDM	Tablets	MWCNT-modified glassy carbon electrode	0.2 - 6.0 μM	13.2 nM	Asiabi et al. (2016)
IDM and acemethacin	Tablets	Mercury electrode	0.0–6.88 ×10^{-8}mM	5.29 mM	Reguera, Arcos, and Ortiz (1998)
Mefenamic acid and IDM	Tablets	Boron-doped diamond electrode	0.3–100 µm	0.4 µm	Petković et al. (2020)
Metoclopramide and IDM	Tablet	ZnFe2O4/MWCNTs-CPE	5.0 -200.0 µM	0.5 µM	Hassannezhad et al. (2019)
IDM	Tablets	Boron-doped diamond electrode (BDDE)	5 – 0.05 mM	0.008 mM	Radovan et al. (2005)
IDM	Tablets	Gr-NiO/GCE	2.0×10^{-7} - 7.0×10-5 mol/L	5.4×10^{-8}mol/L	Liu et al. (2018)
IDM	Tablets	Metrohm EA 290 hanging mercury drop electrode.	1.0--2.0 mM	0.018 mM	Arcos, López-Palacios, and Sánchez-Batanero (1989)
IDM	Tablets	A dropping mercury electrode	5×10^{-9}-5×10^{-8}mol/L	8.1×10^{-10}mol/L	El-Hefnawy et al. (2003)
Dopamine, acetaminophen and IDM	Tablets and ampules	MWCNTs–NHNPs–MCM-41/GCE	0.8-40 µM	0.11 µM	Babaei et al. (2015)
IDM	Tablets	MnO2-Gr/GCE	1.0 × 10^{-7}- 2.5 × 10^{-5} mol/L	3.2 × 10^{-8}mol/L	Liu et al. (2016)
IDM	Tablets and vials	Glassy carbon working electrode (WE)	5 - 50 pg	2 pg	Baudrit and Fabre (1995)
IDM	Tablets	TiO_2 Nanoparticle Modified Carbon Ionic Liquid Electrode	1.0 × 10^{-7} -1.0 × 10^{-4} M	2.1 × 10^{-8} M	Baezzat, Banavand, and Kamran Hakkani (2020)
DantroleneandIDM	Tablets	Hanging mercury drop electrode	0.2–1.2 µg/mL	------	Ragab et al. (2019)
Acemetacinand IDM	Tablets	Mercury thin film modified carbon microelectrode	0.005 - 0.5 mM	1.34×10^{-7} mM	Calado et al. (2013)

Conclusion

This literature review represents an up to date survey about all reported methods that have been developed for determination of indomethacin in its pure form, combined form with other drugs, combined form with degradation products, and in biological samples such as liquid chromatography, spectrophotometry, spectroflourimetry, electrochemistry, etc.

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