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Review Article

Pharmacological and Analytical Profile of Celecoxib

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ABSTRACT

Celecoxib is a selective COX-II inhibitor drug that is used as an anti-inflammatory, analgesic, and antipyretic drug. In this literature review, we will shed the light on its pharmacological action beside most of up-to-date reported methods that have been developed for its determination in its pure form, combined form with other drugs, combined form with its metabolites, and in biological samples.

INTRODUCTION

Eicosanoids are one of the local hormones found in many tissues. They have many physiological and pathological actions. One of their most important precursors is arachidonic acid that is liberated from membrane phospholipids and then oxygenated by separate routes via COX and LOX enzyme, or through free-radical pathways, yielding prostanoids, leucotrienes, epoxygenase products and isoprostanes, respectively [1,2].COX enzymes are found as at least three isoenzymes, COX-1, COX-2, COX-3 and also other variant enzymes exist [3,4]. Most of NSAIDs are non-selective that inhibit COX-1 and COX-2 so they have many adverse effects such as GIT adverse effect [5,6]. Nonetheless, coxib class such as celecoxib (Figure 1) are selective inhibitors that were developed to provide a better GI safety and tolerability than other non-selective drugs like ibuprofen and naproxen [6,7] and its chemical name is 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1 H - pyrazol-1-yl] benzenesulfonamide [8,9]. The risk of gastrointestinal events was significantly lower with celecoxib than with naproxen (P=0.01) or ibuprofen (P=0.002); the risk of renal events was significantly lower with celecoxib than with ibuprofen (P=0.004) but was not significantly lower with celecoxib than with naproxen (P=0.19) [6].

Due to the current importance of this drug in treatment of inflammation related to many diseases, this literature focuses on its pharmacology and different analytical methods that have been developed for determination of this drug in different pharmaceutical and biological samples.

PHARMACOLOGY

Celecoxib is an anti-inflammatory, analgesic, and antipyretic drug. The mechanism of action of celecoxib is the inhibition of prostaglandin synthesis mainly through inhibition of COX-2 as compared to the inhibition of COX-1 activity. Celecoxib has been considered as being 375 times more selective for COX-2 than for COX-1 [10]. It is most effective when the pain is related to inflammation [11]. Celecoxib is absorbed

with peak plasma concentration at ~ 3 h (Tmax) after an oral dose administration and its half-life is ~ 11 h [12], metabolized by CYP2C9 [13], and excretedin urine and feces [14]. It is widely used in treatment of osteoarthritis – rheumatoid arthritis [15,16], familiar adenomatous polyposis [17], ankylosing spondylitis [18], and juvenile rheumatoid arthritis [19]. Celecoxib has some cardiovascular side effects such as atherothrombotic effects, myocardial infarction, stroke: lower risk at low doses for short-term treatment [20,21]. It has also some drug interactions such as clopidogrel, lithium, fluconazole, warfarin, human immunodeficiency virus protease inhibitors [13].

COX-2 is upregulated in several adult epithelial cancers and neuroblastomata, and celecoxib was shown to induce apoptosis and to inhibit neuroblastoma growth. Apart from COX-2 inhibition, another function of celecoxib concerns the potential to inhibit cell proliferation and stimulate apoptotic cell death at much lower concentrations than any other coxibs [22].

REVIEW OF ANALYTICAL METHODS

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

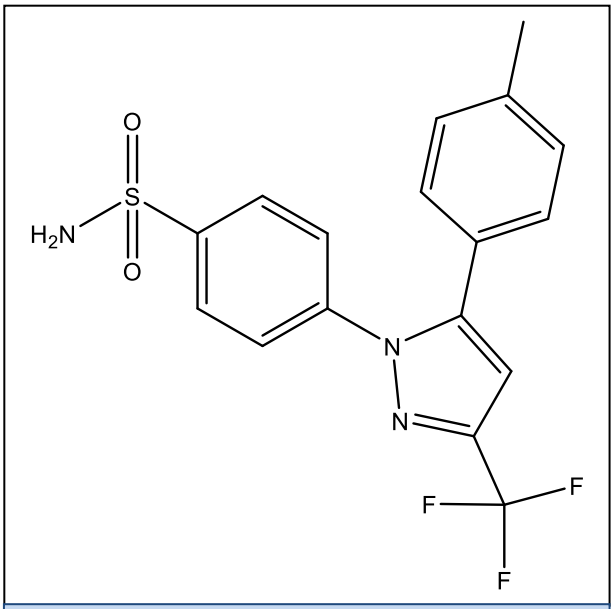

Figure 1: Chemical Structure of Celecoxib.

Spectroscopic methods

Spectrophotometric methods

Drugs	Matrix	Method or reagent	λ_{max}(nm)	Linearity range	LOD	Ref.
Celecoxib	Capsule	UV spectrophotometry	270	20-40 µg/mL	-------	[23]
Celecoxib	Tablet	Ion association complex formation Charge transfer complexation reaction	665 511	0.2-1 µg/mL	0.37 µg/mL 0.426 µg/mL	[24]
Celecoxib	Capsule	UV spectrophotometry	251	1–20 µg/mL	0.26 µg/mL	[25]
Celecoxib and amlodipine besylate	Tablet	Dual-wavelength method Simultaneous equation method	252–357 252	1-25 µg/mL	0.33 µg/mL 0.25 µg/mL	[26]
Celecoxib and amlodipine besylate	Tablet	Vierordt's simultaneous equation method Q-analysis method	255 250	10-50µg/mL	0.343 µg/mL	[27]
Celecoxib and amlodipine	Capsule	First Derivative Spectrophotometric Method Ratio First Derivative Spectroscopy	289.4 286.7	5-40 µg/mL	0.45 µg/mL 0.34 µg/mL	[28]
Celecoxib and amlodipine	Capsule	Absorption correction method Induced dual-wavelength method Fourier self deconvoluted method	253 251-270 269	10-30 µg/mL 5-30 µg/mL 5-30 µg/mL	1.0450 µg/mL 0.6497 µg/mL 0.6737 µg/mL	[29]

Spectrofluorometric methods

Drugs	Matrix	Fluorogenic reagent (method)	λ_{ex} (nm)	λ_{em} (nm)	Linearity range	LOD	Ref.
Celecoxiband flurbiprofen	Capsule	Water	256	403	50-1000 ng/mL	4.97 ng/mL	[30]
Celecoxib	Capsule	Ethanol acetonitrile	272±3	355±5	0.13–2.00 mg/L 0.19–2.32 mg/L	0.04 mg/L 0.06 mg/L	[31]

Chromatographic methods

HPLC methods

Drugs	Matrix	Column	Mobile Phase	Detector	Linearity range	LOD	Ref.
Celecoxib	Human plasma	Luna HILIC column (50 mm × 2.0 mm, 3 µm, Phenomenex, USA)	Formate buffer (pH3.0):methanol (5:95, v/v)	MS/MS	10-2000 ng/mL	3.03 ng/mL	[32]
Celecoxib, hydroxycelecoxib and celecoxib carboxylic acid	Rat plasma	Atlantis T3 column (2.1 mm × 100 mm, 3 µm, Waters, USA)	Ammonium formate : 5% or 95% acetonitrile	MS/MS	5-4000 ng/mL	1.51 ng/mL	[33]
Celecoxib, Erlotinib, and Desmethyl-Erlotinib	Rat Plasma	C_{18} column (50mm × 4.6mm, 3µ, YMC®-PACK, JAPAN)	Methanol: ammonium acetate buffer (80:20, v/v)	MS/MS	1.8-1289.2 ng/mL	0.45 ng/mL	[34]
Celecoxib	Human plasma	Shim Pack GLC-CN, C_{18} column (150 mm×6 mm, 5 µm)	Acetonitrile:1% acetic acid (4:1)	MS	50-1000 ng/mL	20 ng/mL	[35]
Celecoxib	Human and rat plasma	NucleosilRP C_{18} column (30 x 2 mm, 5 µm)	Acetonitrile:water :ammonium hydroxide solution (65:35:0.1, v/v/v)	MS/MS	0.25-250 ng/mL	0.075 ng/mL	[36]
Celecoxib, amlodipine and 4-methylacetophenone	Tablet	ZORBAX Eclipse Plus C_{18} column (4.6 mm × 100 mm, 3.5 µm)	Methanol:formic acid (95:5 v/v)	MS/MS	0.001–50 µg/mL	0.00027 µg/mL	[37]
Celecoxib	Human plasma	ACE C_8-300 column (50 × 4.0 mm, 3.0 µm)	Methanol: ammonium acetate 80:20 (v/v)	MS/MS	10.0-4000 ng/mL	2.50 ng/mL	[38]
Celecoxib and amlodipine	Tablet	Thermo ODS Hypersil C_{18} column (4.6 × 250 mm, 5 µm)	Acetonitrile: potassium phosphate buffer (pH 5.5) 60:40 (v/v)	Fluorescence detector(λ_{ex}265 and λ_{em}359 nm)	0.05-10 µg/mL	0.0167 µg/mL	[39]
Celecoxib and docetaxel	Rat plasma	C_{18} µ-Bondapack column (250 mm × 4.6 mm, Waters)	Acetonitrile:water (45:55, v/v)	UV detector at230 nm	0.05-4 µg/mL	0.015µg/mL	[40]
Celecoxib	Porcine skin	LiChrospher RP-C_{18} column (10 cm, 5 µm, 4 mm)	Methanol:water(72:28, v/v)	UV detector at 251 nm	0.1-3.0 µg/mL in the AS layer 5.0-50.0 µg/mL inSC layer and [EP + D]	0.1 µg/mL	[41]
Celecoxib and	Capsule	Inertsil ODS 3V	Gradient mobile phase Solution A (pH	UV detector at	10-40	0.021 to	[42]

diacerein		column (250 × 4.6 mm; 5 µm, GL Sciences, Inc., Japan)	= 2.3 buffer) and Solution B (methanol and acetonitrile; 50 : 50, v/v)	255 nm	µg/mL	0.027 µg/mL	
Celecoxib and repaglinide	Rat plasma	Kinetex C_{18} column (250 × 4.6 mm, 5 µm, 100 Å)	Acetonitrile: phosphate buffer pH 6.0.	Fluorescence detector (λ_{ex}240 and λ_{em} 380 nm)	10-2000 ng/mL	3.03 ng/mL	[43]
Celecoxib	Human plasma	Nova Pak C_8 column (3.8 × 150 mm,	Acetonitrile: tetrahydrofuran: 0.02M sodium acetate buffer (30:8:62)	UV detector at 252 nm	40–4000 ng/mL	12.12 ng/mL	[44]
Celecoxib	Human plasma	Nucleosil-NO_2 column (150 x 4.6 mm, 5 µm)	Hexane:methylenechloride:isopropyl alcohol (70:25:5, v/v).	UV detector at 260 nm	25-2000 ng/mL	7.57 ng/mL	[45]
Celecoxib	Human Serum	Prontosil C_{18} AQ column (150×3 mm, 3µm)	Water:acetonitrile (40:60, v/v)	Fluorescence detector (λ_{ex}240 and λ_{em} 380 nm)	12.5-1500 ng/mL	3.78 ng/mL	[46]
Celecoxib and rofecoxib	Human plasma	Zorbax SB-CN (5 µm) column	Acetonitrile: potassium dihydrogen orthophosphate buffer pH 2.4 (42:58, v/v)	UV detector at 254 nm	20-2000 µg/L	6.06 µg/L	[47]
Celecoxiband doxorubicin	Nanoparticulate fixed dose combination (NanoFDC)	Inertsil ODS-3 C_{18} column (250 mm x 4.6 mm, 5 µm)	Acetic acid (pH 3.0, 1 %): acetonitrile(40:60 v/v)	Fluorescence detector (λ_{ex}480 and λ_{em} 590 nm)	1-11 µg/mL	13 ng/mL	[48]
Celecoxib	Human plasma	Knauer C_{18} column (4.6 mm. x 250 mm, 5 µm)	Acetonitrile:water (75/25, v/v)	UV detector at 250 nm	0.2–2000 µg/L	0.08µg/L	[49]
Celecoxib	Human plasma and breast milk	Aqua C_{18} (75 mm × 4.6 mm 5 µm)	Acetonitrile: phosphate buffer pH 3.5 (50:50, v/v) containing 0.1% triethylamine	UV detector at 254 nm	10-2000 µg/L	3.03 µg/L	[50]
Celecoxib, etoricoxib, salicylic acid, valdecoxib, ketoprofen, nimesulide	Human plasma	Kromasil KR 100-5 C_{18} column (4.6 x 250 mm, 5 µm)	Gradient mobile phase Formic acid (pH 3): acetonitrile:methanol:water	UV detector at 235 nm	0.1-50 µg/mL	0.03 µg/mL	[51]
Celecoxib	Human plasma	Monolithic silica column (RP-18e, 100 mm × 4.6 mm)	Acetonitrile:methanol: distilled water (45:10:45, v/v/v) containing 0.2% acetic acid (pH 3.5)	UV detector at 254 nm	10-800 ng/mL	3.03 ng/mL	[52]
Celecoxib	Human plasma	Nucleosil C_8 column (120-5, 11 x 2 mm)	----------	UV detector at 253 nm	5-2000 µg/L	1.5 µg/L	[53]
Celecoxib, hydroxycelecoxib, and carboxycelecoxib	Human plasma	Phenomenex Luna C_{18} column (5 µm, 150×4.6 mm)	Gradient mobile phase acetonitrile:sodium hydrogen phosphate buffer (pH5.4)	UV detector at 254 nm	10-500 ng/mL	3.03 ng/mL	[54]
Celecoxib, alprazolam and diclofenac sodium	Tablet and human serum	Shimadzu Shim-pack CLC-ODS 25M column (4.6 mm × 0.25mm)	Methanol: water (pH 3.5) (80:20,v/v)	UV detector at 230 nm	0.3-20 µg/mL	17.29 ng/mL	[55]
Celecoxib	Human plasma	Nucleosil 100-5 CN column (5 µm, 250×4.6 mm)	Acetonitrile:water (60:40 (v/v))	UV detector at 260 nm	10-1000 ng/mL	3.03 ng/mL	[56]
Celecoxib, rofecoxib, valdecoxib, nimesulide and nabumetone	Tablet and human serum	Inertsil C_{18} column (5 µm, 250×4.6 mm)	Methanol:glacial acetic acid (68:32, v/v)	UV detector at 230 nm	1-20 µg/mL	1.040 µg/mL	[57]

HPTLC methods

Drugs	Matrix	Stationary phase	Mobile phase	Detector	Linearity range	LOD	Ref.
Celecoxib, amlodipine and 4-methylacetophenone	Tablet	Silica gel 60F_{254} plates	Methanol: water: ammonia (70:25:1.5, v/v/v)	UV at 264 nm	1–150 µg/band	0.291 µg/band	[37]
Celecoxib	Capsule	Silica gel 60F_{254} plates	n-hexane–ethyl acetate, 60 + 40 (v/v)	UV at 262 nm	200 - 2000 ng	------	[58]
12 NSAIDS drugs	Urine	Silica gel 60F_{254} plates	Ethyl acetate–toluene–methanol–acetic acid 40:40:1:1 (v/v)	UV at 254 nm	0.5–5 µg/spot	0.005-0.5 µg/spot	[59]
Celecoxib, piroxicam, tenoxicam, and rofecoxib	Human whole blood and urine	Silica gel F_{254} plates	Ethyl acetate–toluene–butylamine (2 : 2 : 1, v/v/v) and chloroform–acetone–toluene (6 : 2.5 : 1, v/v/v)	UV at 254 nm	2.8 - 38.6 µg/mL	0.06 µg/mL	[60]

Electrochemical methods

Drugs	Matrix	Electrode	Linearity range	LOD	Ref.
Celecoxib	Capsule and human serum	Mercury electrode surface in Britton–Robinson buffer of pH 7.0	1×10^{-9}–2×10^{-8} M	1.86×10^{-10} M	[61]
Celecoxib	Tablets	Graphene Based Carbon Ionic Liquid Electrode Modified with Gold Nanoparticles	0.5-15 µM	0.2 µM	[62]
Celecoxib	Tablet and human serum	Pencil graphite electrode (PGE) modified with functionalized multi-walled carbon nanotubes (MWCNTs).	5.0×10^{-3}–20 µM	2.34×10^{-3} µM	[63]
Celecoxib	----------	Polyaniline grafted multiwall carbon nanotubes modified electrode	1×10^{-11}–1×10^{-6} M	----------	[64]

CONCLUSION

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

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