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Review Article

A concise review on analytical profile of naproxen

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Abstract

Naproxen (NAP) is a Non-steroidal anti-inflammatory drugs (NSAID) used in the treatment of pain or inflammation caused by situations such as arthritis, ankylosing spondylitis, tendinitis, bursitis, gout, or menstrual cramps. Nap is available in isolated dosage from with various similar anti- inflammatory drugs, esomeprazole, pantoprazole, paracetamol, ranitidine, sumatriptan and ibuprofen. The present exploration evaluates the various method for analysing of NAP in bulk drugs and formulated products. A summarizing review characterizes the gathering and conversation of about more than 62 analytical methods which includes HPLC, HPTLC, UV-Spectrophotometry, capillary electrophoresis, electrochemical methods. HPLC technique are provided in Table03 and Table 04 for NAP alone and combination, including parameters such as matrix, stationary phase, mobile phase, wavelength detection etc. and HPTLC methods are reported in Table 05 with parameters like stationary phase, mobile phase combination, R_F etc. Method of UV-Spectrophotometry applied for examination of NAP in biological mediums, bulk sample and in various dosage formulation. Spectrometric methods for NAP alone and in mixture are given in Table 08 which includes parameters like λ max, solvent, matrix etc.

Keywords: Naproxen, HPLC, HPTLC, UV-Spectrophotometric, LC-MS/MS.

Introduction

Naproxen is a structurally [(S)-6-methoxy-alpha-methyl-2-naphthaleneacetic acid] action has non-steroidal anti-inflammatory medicine that shows both antipyretic and analgesic behavniour.[1] Naproxen formulation is Artagen, Arthopan and Napexar formed by Ranbaxy.

The mechanism action of naproxen, similar to that of other NSAIDs, has believed to be related with Cyclooxygenase activity inhibition.COX-1 inhibition should be complementary to gastrointestinal and renal toxicity while COX-2 inhibition is anti-inflammatory.[2] Similar to added NSAIDS naproxen is capable of creating troubles in the gastro intestinal tract naproxen is practically insoluble in water, soluble in ethanol 96 percent and pka in methanol 4.2.[3] Naproxen is generally metabolized to 6-0-desmethyl naproxen and mutually parent and metabolized do not produce metabolizing enzymes. The practically observed incurable exclusion half-life is almost 15 hours. Naproxen is normally used for the reduction of fever, pain also inflammation and stiffness caused by in conditions including of osteoarthritis, migraine, rheumatoid arthritis, psoriatic arthritis, kidney stone, gout, kidney stone, menstrual cramps,ankylosing spondylitis, tendinitis and bursitis.[4]

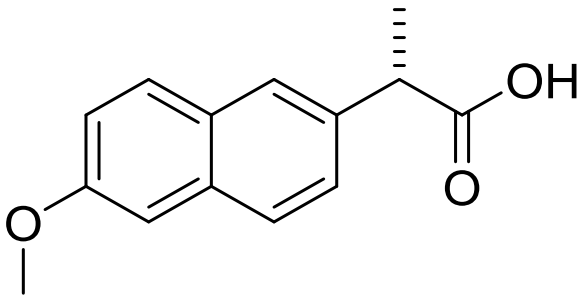

Fig. 1: Chemical structure of Naproxen

Mechanism of action

The mainly mechanism action of naproxen is its inhibition of production prostaglandin of by binding reversibly to cyclooxygenase. This have first enzyme in the arachidonic acid cascade that results in the synthesis of prostaglandins. By lowering the levels of these abundant substances, naproxen affects pain, inflammation, fever, uterine contractility, platelet aggregation, and vasoactivity, all of which are mediated by prostaglandins and related thromboxanes and prostacyclin. All non-steroidal anti-inflammatory preparations appear to act same by blocking the cyclooxygenase stage in the cascade.[5]

Pharmacokinetic data

Bioavailability

Naproxen is one of the fastly and completely produced in the GI tract with an in vivo bioavailability of 95%. Although naproxen itself is good absorbed, the sodium salt form is more speedily absorbed resulting in greater

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maximum plasma concentration at specified dose. Food causes a minor decrease inabsorption rate.

Protein binding
Therapeutic levels of Naproxen>99% albumin-bound.

Metabolism
Naproxen and Parent as well as and metabolites do not couse enzyme metabolizer. Naproxen is widely metabolized to 6-0-desmethyl

Half-life
The practically observed elimination of half-life is approximately 15 hours.

Excretion
0.13 mL/kg clearance of naproxen. Almost 95% of the naproxen from any dose is excreted in the urine, mostly as naproxen (Less than 4%), 6-0-desmethyl naproxen (less than 1%) or their conjugates (66% -92%).

Clinicaluse
Naproxen if used to relive pain from various circumstances, including headaches, muscle aches, tendonitis, dental suffering, and cramps of menstruation. It also decreases arthritis, bursitis, and gout assaults pain, inflammation, and joint stiffness.

Adverse effects
Naproxen was correlated with the lowest general cardio vascular risk of all the NSAIDs assessed.
As with other NSAIDs, naproxen may trigger gastrointestin al issues such as heartburn, constipation, diarrhea, ulcers, an d swelling in the stomach. It may interfere with and decreas e the efficacy of SSRI antidepressants.[6]

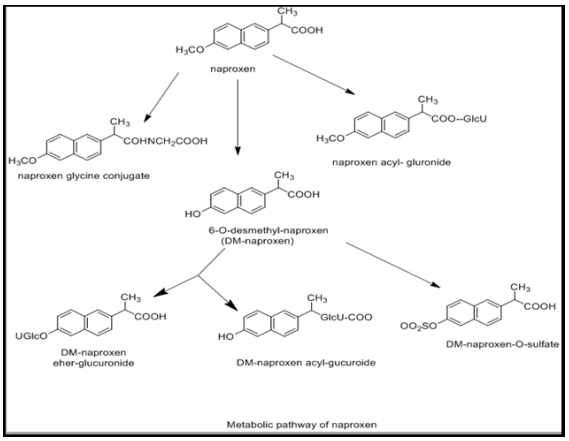

Fig. 2: Metabolite pathway of naproxen

Metabolite
The 6-O-desmethylated metabolite (DM-naproxen) is unchanged excreted and combined with sulfate and glucuronic acid The 6-O-desmethylated metabolite (DM-naproxen) is excreted unaffected as well as combination with glucuronic acid and sulphate.[7]

Analytical accounts on naproxen
The general literature survey discovered, several analytical method viz UV/Visible- Spectrophotometry, Spectrofluorimetry, HPLC, HPTLC and LC-MS for the resolve of NAP in bulk and pharmaceutical product. The recorded methods describe the determination of naproxen in different dosage forms as single component and in mixture with esomeprazole, domperidone, sumatriptan succinate, pantoprazole, rabeprazole, pseudoephedrine, paracetamol, ranitidine hydrochloride, diphenhydramine hydrochloride. Fig. 4 shows different analytical methods implemented for assessment of naproxen.[8]

Analytical method for Naproxen

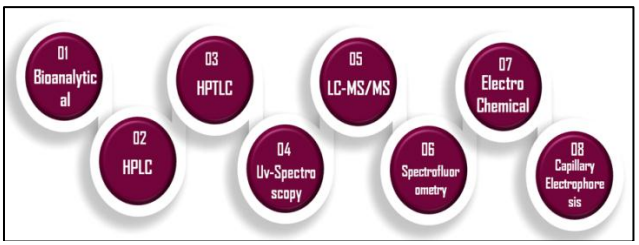

Fig. 4: Analytical accounts on Naproxen

Table 1: Dosage forms, route of administration and recommended dose of NAP

Dosage forms	Route of administration	Indication/dose
Tablet and suspension		Usual Adult Dose of Ankylosing Spondylitis- 250 mg to 500 mg (naproxen) or 275 mg to 550 mg (naproxen sodium)twice daily orally
Tablet and suspension		Usual Adult Dose of Rheumatoid Arthritis-250 mg to 500 mg (naproxen) or 275 mg to 550 mg (naproxen sodium) twice daily orally
Tablet		Usual Adult Dose for Acute Gout-750 mg

Tablet	Oral	Usual youth dose of paediatric Rheumatoid Arthritis-older than 2 years: 5 mg/kg orally twice a day
Tablet and suspension		Usual Adult Dose for Osteoarthritis-250 mg to 500 mg (naproxen) or 275 mg to 550 mg (naproxen sodium) twice daily orally
Tablet and suspension		Usual Pediatric Dose for Childish Rheumatoid Arthritis-

Pharmacopoeial status

IP portrayed HPLC assay technique consuming a stainless steel 25 cm x 4.6 mm, packed with silica gel π-acceptor/π-donor for chiral separations (5µm), as a static phase and mobile phase comprised of 5 volumes of a glacial acetic acid, 50 volume of acetonitrile, 100 volume of 2-propanol and 845 volume of hexane, keeping the flow rate of 2 mL/min. Column effluent was scrutinized on 263 nm, and injection volume set at 20 µl.[9]

Accounts on bio-analytical method for estimation of naproxen

Bio-analysis is a sub-discipline of analytical chemistry casing the quantitative dimension of xenobiotics and biotic (proteins, macromolecules, DNA, metabolites, molecule of drugs,) in biological systems.[10]

Literature survey exposed that HPLC is predominantly used for the bio-analysis of Naproxen

S. Ashutosh Kumar et al (2014) was studied the bioanalytical RP-HPLC technique for simultaneous purpose of ESOM and NAP in human plasma was established and validated as per US-FDA guidelines, by consuming symmetry C18 (250 mm×4.6mm, 5 250 mm, 5 µm) XTerra column and potassium dihydrogen phosphate and acetonitrile with mobile phase portion of 60:40 v/v at a pour rate of 1.0ml/min. 1.0-6.0 µg/ml concentration range was selected for ESOM and NAP 25.0-150.0 µg/ml, and 0.999 correlation coefficient of both drugs respectively ESOM and NAP. The assay of allowable measurement of ESOM and NAP was found to be 0.04µg/ml both drugs. The average recovery for the drug ESOM and NAP was found to be 98.97-99-84 and 99.80-100.95.[11]

Bilal Yilmaz et al. (2013) recognized a validated simple HPLC tecnique has been recognized for the resolution of NAP in human plasma. The detection was accomplished on an Ace C18 column using UV-Detection. The mobile phase having of 20mm phosphate buffer (pH7) containing 0.1% trifluroacetic acid: acetonitrile (65:35) v/v and The linearity was reliable in series of 0.10 and 5.0 mg/ml. precision (intra-day, inter-day)correctness morals for NAP in plasma were less than 4.84, and accuracy (reasonable error) was better than 3.67%.

Nap's extraction percent retrieval trials since human plasma were discovered to be 91.0 and 98.9%. The LOD and LOQ weredicoverd to be 0.03 and 0.10 mg/ml, respectively. This assaywas also helpful in regulating NAP pharmacokinetic variables in six energetic Turkish volunteers who needed to remain given 220 mg of NAP.[12]

Table 2: Bio-Analytical NAP technique

S. No.	Drug	Sample Matrix	Method	Column	Detection	Internal Standard	Ref
1.	NAP	Human plasma	HPLC	C18	-	Ibuprofen	12
2.	NAP	Human plasma	HPLC	C18	254nm	ACN (Human Plasma)	13
3.	NAP, IBFN and PARA	Human plasma	HPLC-UV	Zorbax SB-C18	232nm	Fenoprofen	14
4.	NAP and ESOM	Human plasma	LC-MS/MS	XBridge C18	-	Ibuprofen	15
5.	Atenolol, Rosuvastatin, Spironolactone Glibenclamide and NAP Sodium	Human plasma	RP-HPLC	C18	235nm	Flurbiprofen	16
6.	NAP	Human Urine	HPLC	C18	-	-	17
7.	ESOM and NAP	Human plasma	RP-HPLC	C18	285nm	-	18
8.	NAP	Human plasma	LC-MS/MS	-	-	Ketoprofen	19
9.	NAP	Human plasma	LC-MS/MS	C18	-	Zidovudine	20
10.	NAP and BPB	Human Serum	Spectrophotometry	-	432 nm	-	21

Chromatography overview

HPLC [High Performance Liquid Chromatography]

In pharmaceutical formulations, apart from pharmacopeial t echniques, many HPLC techniques have been recorded for NAP determination.Table 3 shows the summary of the repor ted HPLC technique specifying the mobile phase used for determination, sample matrix, πmax and linearity.

The instrumentation of HPLC techniques for NAP deter mination is summarized in Table 4. *Sagar D. Solanki et al. (2011).* Reported the simple RP-HPLC tenique were set up and validated for purpose of NAP sodium and SUM succinate in dosage form tablet. The mobile phase system is a blend of H_2O: ACN (60:40 v/v) and 0.5% trifluro acetic acid was added in water, and flow rate of 1.0ml/min. The keeping wavelength of PDA detector at 277 nm. For both drug, a linear calibration curve is began in the 5-80µg / ml concentration sequence.

The technique has been validated for parameters such a s specificity, accuracy, precision and linarity. The percent recovery was discovered to range from 98.0% to 102.0% to the marked value. The presented method was used efficiently for repeated quantitative analysis of tablets contai ning naproxen and sumatriptan.[22]

Md. Shozan Mondal et al. (2011) Reported the easy, sensitive and specific RP-PLC technique for assessing NAP and DOM in tablet dosage form,, accomplished with a shim-pack C18 column (250 mm × 4.6 mm 5 µm), with a movable phase system is a blend of phosphate buffer: methanol (30:70 v/v), (pH attuned to 3.00 with sodium hydroxide), at a flow rate of 1.0 ml/min using UV finding at 280 nm. The proposed technique is found to be having linear correlation coefficient of r^2 =0.999 for NAP and DOM), exact with 99.5% recovering for DOM and 99.39% recovery for NAP and precise (%RSD ≤1%). This method used for the identify potency of profitable product and potency was found within limit. The technique can be used in tablet dosage for NAP and DOM assessment.[23]

Table 3: HPLC Method for Naproxen (NAP)

S. No	Drug	Method	Matrix	Column	Mobile Phase	Flow rate	Detector	Rt	Ref
1	NAP	RP-HPLC	Bulk	C18	Phosphate Buffer and Methanol 40:60 (v/v).	1.3 ml/min	UV-Detector	NAP-5.82	24
2	NAP	HPLC	Tablet	-	Acetonitrile and 10 mm Ammonium acetate buffer pH 3.8 in ratio 550:450 v/v (pH 3.8 adjusted with acetic acid)	1.0 ml/min	-	5.9 ± 0.01 min.	25
3	NAP	RP-HPLC	Dosage form	C18	Acetonitrile:0.5 M potassium dihydrogen phosphate buffer pH 2.5 adjusted with ortho-phosphoric acid: tetrahydrofuran (45:53:2 v/v/v).	1.0 ml/min	UV-Detector	3.25 min.	26
4	NAP	RP-HPLC	Bulk and Tablet	C18	Ammonium acetate Buffer: Methanol 40:60 (v/v)	1.0 ml/min	UV-Detector	3.063	27
5	NAP	UHPLC	Bulk	C18	-	1.0 ml/min	UV-Detector	-	28

Table 4: HPLC methods for analysis of Naproxen in combination

S. No	Drug	Method	Matrix	Colum n	Mobile Phase	Flow rate	Detector	Rt	Ref
1	SUMA and NAP	RP-HPLC	Tablet	C18	ACN: Water (60:40) and 0.05% v/v.	1 ml/min	PDA Detector	SUMA 2.26 NAP 5.79	29
2	NAP and ESOM	HPLC		C18	Phosphate buffer (pH 6.1) and acetonitrile in ratio of (40:60, v/v.	1.5 ml/min	UV Detector	NAP 1.72 ESOM 2.29	30
3	DOM and NAP	RP-HPLC		C18	Phosphate buffer (pH adjusted to 3.00 with sodium hydroxide): methanol in the ratio 30:70 (v/v)	1.0 ml/min	UV Detector	DOM-3.17 NAP-5.42	31
4	NAP and	RP-	-	C18	Phosphate buffer (pH 6.5	1.0	UV Detector	DOM-	32

	DOM	HPLC			adjusted with orthophosphoric acid) and acetonitrile in the ratio of 50:50 (v/v)	ml/min		2.63 NAP-4.27	
5	NAP and ESOM	RP-HPLC	-	-	Acetonitrile: Methanol in the Ratio of 60:40 (v/v).	1.0 ml/min	UV-Detector	ESOM-3.425 NAP-4.352	33
6	SUMA and NAP	RP-HPLC	Bulk and Tablet	C18	Water: Methanol in The ratio of 55:45 (v/v)	1.0 ml/min	UV-Detector	SUM-2.90 NAP-3.480	34
7	NAP and PAN	RP-HPLC	Capsule	C18	Phosphate buffers (K2HPO4,KH2PO4) (PH:6.5) Acetonitrile (55:45 v/v)	1.0 ml/min	-	NAP-3.357 PAN-4.907	35
8	NAP and PAN	RP-HPLC	Capsule	C18	Methanol: phosphate buffer (5.4) in the ratio of 70:30 (v/v).	1.0 ml/min	PDF-Detector	NAP-3.33 PENTO-1.90	36
9	ESOM and NAP	RP-HPLC		C18	Acetonitrile: Phosphate buffer (pH7.0) in the ratio Of 50:50 (v/v)	0.5 ml/min	PDF-Detector	ESO-	37
10	NAP and ESOM	HPLC		C18	Buffer: Acetonitrile: Methanol = 50:40:10 add 0.1% v/v Triethylamine in above mixture and finally adjust with glacial acetic acid to a pH 7.0.	1.0 ml/min	UV-Detector	-	38
11	NAP and ESOM	RP-HPLC	Tablet	C18	Buffer, Acetonitrile and Methanol in the ratio of (70:20:10) v/v/v.	1.5 ml/min	UV-Detector	NAP-3.352 ESO-6.112	39
12	NAP and RAB	RP-HPLC	Bulk	C18	Sodium dihydrogen Buffer: Acetonitrile in the ratio of 70:30 (v/v)	1.0 ml/min	UV-Detector	NAP-3.33±0.027 RAB-7.61±0.043	40
13	NAP and SUMA	RP-HPLC	Bulk and Dosage form	C8	Buffer: Acetonitrile In the ratio of 50:50 (v/v)	0.7 ml/min	UV-Detector	NAP-2.249 SUM-5.875	41
14	NAP and PEPH	HPLC	-	Spheriso-rb Cyano	Water: acetonitrile–Methanol: triethylamine mixture in the ratio of 850:75:75:5(v/v).	0.5 ml/min	UV- Detector	NAP-Na 1.11 PSEH-0.39	42
15	SUMA and NAP	RP-HPLC	Bulk and Dosage form	C18	Acetonitrile: Methanol: phosphate buffer in the ratio of 50:10:40 (v/v).	1.0 ml/min	-	NAP-4.037 SUM-2.813	43
16	SUMA and NAP	UPLC	-	C18	Acetonitrile: Water In the ratio of 90:10 (v/v).	1.0 ml/min	UV-Detector	SUM-1.7 NAP-2.7	44
17	PARA and NAP	RP-HPLC	Tablet	C18	Water: Acetonitrile in the ratio of 87:13 (v/v)	1.0 ml/min	UV-Detector	PARA-3.005 NAP-7.402	45
18	ESOM and NAP	RP-HPLC	Bulk and Tablet	C18	Phosphate buffer (pH 3) and Acetonitrile	1.0 ml/min	DAD and UV Detector	ESO-2.105	46

					60: 40 (v/v).			PAN-3.555	
19	DIFL and NAP	HPLC	Tablet	C18	Acetonitrile: Acetate buffer (pH 4.2; 50 mm) (60:40, v/v).	0.7 ml/min	UV-VIS Detector	-	47
20	RAN, DOM and NAP	RP-HPLC	-	-	0.1 M Orthophosphoric acid solution (pH 3.0): methanol (35:65 v/v)	1.0 ml/min	UV-Detector	RAN-2.702 DON-3.666 NAP-9.842	48
21	NAP and PEPH	HCL	Tablet	C18	0.2 M acetate buffer and Acetonitrile (40: 60) (v/v).	1.7 ml/min	PDA Detector	NAP-5.87 PSE-1.345 IS-2.91	49
22	NAP and ESOM	RP-HPLC	Tablet and Dosage form	C18	Buffer [tetrabutylammonium hydroxide and n-heptane sulfonic acid–Na salt acetonitrile and methanol in a 60: 20: 20 v/v/v ratio	1.0 ml/min	UV-Detection	NAP - 4.9±0.1 min, ESP 6.8±0.1 min.	50
23	EOME and NAP	RP-HPLC	Bulk and Tablet	C18	Acetonitrile: potassium dihydrogen phosphate buffer (60:40 v/v).	1.0 Ml/min	UV-Detector	ESO-3.052 NAP-6.140	51
24	NAP and DIPH HCL	RP-HPLC	Bulk and Tablet	C18	15mM ammonium acetate buffer: Acetonitrile (60:40V/V).	1.0 ml/min	PDA-Detector	NAP 4.49 DPH 10.80	52

High performance thine layer chromatography (HPTLC)

Six easy HPTLC techniques were studied for simultaneous NAP estimation in mixed dosage from with SUMA, PAN, DOM and DIPHY. Table 5 shows the overview of the reported HPTLC techniques.

Riddhi Gondalia et al. (2011) created and validated a straightforward mixed dosage technique for NAP and SUMA, a co nventional NAP and SUMA solution for percolated silica gel 60F 254, and a mobile phase for methanol growth: distilled wat er: formic acid ratio of 0.5:7.5:0.1 (v/v/v), The accuracy and precision of the suggested technique were analysed by the recovery study and the% recovery for SUMA was 99.255 and 99.0.3% respectively, and behind development, plates were observed under UV light. The detector response for NAP sodium and SUMA succinate was linearity in the range of 200-1200 ng / spot and 100-1000 ng / spot.

Shubhangi M. Pawar (2010), Investigation of a easy, accurate and precise high-performance thin-layer chromatography technique for simultaneously quantify action of DOM-S and NAP-S as bulk drug and in tablet dosage form. The stationary phase was carried out on aluminum plates pre-coated with silica gel 60F 254, and mobile phase was toluene: methanol: acetone (8: 2: 2, v/v/v), and Rf value was found to be 0.44±0.02 and 0.5 ± 0.02 for DOM-S and NAP-S, respectively. The densitometric scanning was done at 266 nm. The linearity range was chosen by 20–140 ng. spot-1 for DOM and 500-3500 ng. spot-1 for NAP,), precision (intra-day RSD0.4–1.01% and inter-day RSD 0.316–0.876% for DOM, and intra-day RSD 0.488–1.329% and inter-day RSD 0.450–1.026% for NAP), and accuracy (98.38 ± 0.55% for DOM and 98.64 ± 0.49% for NAP), specificity, in accordance with ICH guidelines.[54]

Table 5: HPTLC Method for determination of Naproxen

S. No	Drugs	Matrix	Stationary phase Plates	Mobile phase composition	Detection (nm)	Linearity	Rf	Ref
`1	NAP and SUMA	Dosage form	Silica gel 60F254	Methanol: distilled water: formic acid in the capacity ratio of 0.5:7.5:0.1 (v/v/v),	230 nm	(200-1200 ng/spot) NAP (100-1000 ng/spot) SUMA	-	53
2	DOM and NAP	Bulk	Silica gel 60 F254	Toluene: Methanol: acetone (8: 2: 2, v/v/v).	266 nm	20-140 ng.spot -DOM 500-3500 ng.spot-	-	54

						1- NAP		
3	NAP and PAN	Bulk and tablet	Silica gel 60 F254	Ethyl acetate: glacial acetic acid (4.8:0.2).(v/v)	310 nm.	NAP- 50 to 300 ng/spot PENTO 250 to 1500 ng/spot	NAP- 0.67 PENTO- 0.3	55
4	DPH HCL and NAP	Tablets	Silica gel 60 F254	Toluene: methanol: glacial acetic acid (7.5:1:0.2, v/v/v).	230 nm	-	-	56
5	NAP and PAT	Capsule dosage forms	Silica gel F254	Toluene: Chloroform: Methanol: Formic acid (3:5:2.1:4.2:0.2, v/v/v).	241 nm	**NAP-** 25-125 µg/ml PAN- 4-20 µg/ml	**NAP-** 0.41 ± 0.02 PAN- 0.51 ± 0.02	57

Spectrophotometry methods

Till the date, the UV-Spectrophotometry methods for determination of NAP alone and in one or more dosage forms. The Spectrofluorimetry methods have been investigated analysis of NAP in tablets. The details Spectrophotometry and Spectrofluorimetry designating the basic principle, sample matrix, λmax and solvent and linearity range are concise in Table 8.

Methods for analysis of NAP as a single component

*Senthil Rajan Dharmalingam et al.(2013)*The simple, delica te and accurate UVSpectrophotometric technique for definin g NAP in bulk and semisolid formulation was Dignified at 3 31 nm.The lnearity range for NAP was discovered to be 10-60µg/ ml, and the system was validated for various paramet ers such as accuracy, accuracy and specificity as per guideli nes (ICH).Comparative usual deviation and% recovery stan dards have been discovered to be satisfactory, representative that the suggested method is accurate and precise and can b e used later in bulk and semisolid pharmaceutical formulatio n for repetitive NAP investigation.[57]

Methods for analysis of NAP in combined dosage form with other drugs

Along with many anti-inflammatory, histamine and gastrointestinal agents, NAP is applicable. Few UV-spectrophotometry methods were reported for the simultaneous determination of NAP in dosage forms and simple, fast, precise, accurate and economical methods were developed for the evaluation of NAP and PANTO, DOM, PARA, RAN in tablet dosage form.

Asha Patel et al. (2014) For the simultaneous evaluation of NAP and PARA in pharmaceutical dosage form, the easy, Q-absorbance ratio UV-spectrophotometric technique was researched and validated. The chemicals used were NaOH 0.1N. The first scheme of working simultaneous equation solving based on the identification of absorbence at two wavelengths, 257.00 nm (λmax for PARA) and 234.00 nm (Isoabsorptive point) were specific to the approximation of PARA and NAP for the technique of Q-absorbance proportion. To select the isoabsorbent point for evaluation, the overlay spectrum of NAP and PARA drugs was used. The chemicals used were NaOH 0.1N. The first operating system to solve simultaneous equation based on the detection of absorbence at two wavelengths, 257.00 nm (λmax for PARA) and 234.00 nm. linearity of the preferred technique for paracetamol was 2.5-5.0 µg / ml and for naproxen was 1.5-3.0 µg / ml. The%recovery study was found to be corresponding to 97.9 1% (PCM) and 98.64%(NAX). The predicted scheme was a ccurate, selective and accurate in bulk formulation for simul taneous evaluation of NAP and PARA. Naproxen 1.5-3.0 µg / ml. The% recovery study was found to be 97.91% for (PCM) and 98.64% for (NAX) accordingly. The projected tecnique was accurate, selective and precise for simultaneous assessment of NAP and PARA in bulk formulation.[58]

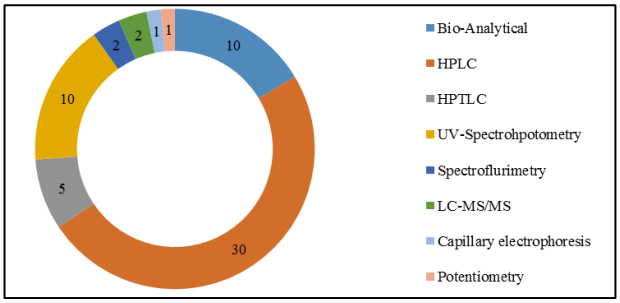

Fig. 6: Percentage Utility of Analytical Approaches used for estimation of Naproxen

Tasnuva Haque et al. (2008) reported that to simple, correct methods for the simultaneous estimation of NAP and RAN and their combined form of UV-Spectrophotometry method were studied and validated. Simultaneous equation technique (SEM) uses NAP and RAN inquiry using 313 nm in pH 7.4 phosphate buffer and 314 nm in 0.1N HCL and H2O as well as NAP investigation at 229 nm in pH 7.4 phosphate buffer and 232 nm in both 0.1N HCL and in H_2O parallel to the specific absorption maxima. The tablet formulations were expected for the percent content of both the drugs at the designated wavelengths and the percent influence were 98.83 and 99.15 for NAP and RAN HCL respectively.[59]

Table 7: Spectrophotometric methods used for determination of NAP alone and in combine dosage form

S. No	Drugs	Matrix	Linearity (µg/ml)	Coefficient Correlation	Accuracy study in (%)	LOD&LOQ (µg/ml)	Ref
1	NAP	Bulk and Semi-solid Formulation	10 - 60µg/ml	0.9984.	80,100,120.	LOD-1.5357µg/ml LOQ-5.1191µg/ml	57
2	NAP and PARA	Bulk	PARA-2.5 – 5.0µg/ml NAP 1.5 – 3.0µg/ml	PARA-0.9996 NAP-0.999	80, 100, 120.	-	58
3	NAP AND RAN-HCL	Tablet	RAN-5-25 µg/ml NAP-0.2-1.25 µg/ml	NAP-0.9976 RAN-¤ 0.997	-	RAN-LOD-75.205 LOQ-250.685 NAP-LOD-1.411 LOQ-4.702	59
4	NAP and DOM	Tablet	NAP-10-35 *µg*/ml DOM-5-30 *µ*g/ml	NAP-0.9999 DOM-0.9998	80, 100, 120.	NAP-LOD 0·454 *µ*g/ml DOM-LOD 0.657 mg/ml NAP-0·151 *µ*g/ml DOM-2.18 mg/ml	60
5	NAP	Tablet	NAP-20-140 µg/ml	NAP-• 0.999	80,100,120.	-	61
6	LNP and NAP	Tablet	LAN-5-30µg/ml NAP-10-35µg/ml	LAN-(0·998) NAP-(0·999)	80,100,120.	NAP-LOQ 0·15µg/ml LAN-LOQ 1·7µg/ml. NAP-LOD 0·04µg/ml LAN –LOD 0·5µg/ml.	62
7	SUMA-S and NAP- S	Tablet	3-18 ppm for both the drugs.	-	80, 100, 120.	LOD-NAP-0.24 SUM-0.31 LOQ NAP-0.74 SUM-0.94	63
8	NAP and PAN	-	NAP-10.0- 50.0 µg/ml PANTO-8.0- 18.0 µg/ml	NAP-0.998 PAN-0.996	-	-	64
9	NAP-S and PAN-S	Bulk and dosage form	NAP-02-10 µg/ml PAN-02-10 µg/ml	NAP-0.995 PAN-0.995	NAP-80, 100, 120. PAN-(6.4, 8, 9.6)	NAP-0.011 µg/ml, 0.0042 µg/ml, PAN-0.0042 µg/ml, 0.0129 µg/ml	65
10	ESOM and NAP	Bulk and tablet dosage form	ESO-5-50µg/ml NAP-5-50µg/ml	ESO-0.9993 NAP-0.9995	80, 100, 120.	-	66

Spectrofluorimetric methods

Alberto Navalo´n et al. (1998) reported the different Spectrofluorimetry method, depend on measurement of native fluorescence intensity of both drugs at emission 300 nm and 520 nm is using excitation wavelength of 290 nm. The excitation–emission spectra of these compounds are powerfully overlapped, which doesn't authorize their direct. The concentration range was discover to be 0.1-1.0µg/ml for NAP and 0.5-5.0 µg/ml for SA and 2.0-12.0 µg/ml for ASA. To validate the accurateness of the expected technique, the improved model, obtained by PLS-1, was useful to the purpose of these compounds in pharmaceuticals and human

serum samples earlier spiked with dissimilar amounts of each chemical.[67]

Patricia Damiani et al. (2002) defined a simple, sensitive and reliable Spectrofluorimetry technique for determination of Naproxen in tablets.

The fluorescence concentration was discovered to be 35 3 nm using an excitation frequency of 271 nm, and in order t o validate the scheme the effects were contrasted with those acquired by the USP XXIV NF 19 Pharmacopoeia reference technique (HPLC). In this concluding case a modification process is necessary.[68]

Liquid chromatography–mass spectrometric methods

Shanmugam Gopinath et al (2013) studied validated a simple fast method simultaneous analysis, in human plasma of NAP and ESOM using high performance liquid chromatography-tandem mass spectroscopy (LC-MS/MS). Solid-phase extraction was used to obtained analyte and internal standard from human plasma, and differentiation of analyte and internal standard was accomplish on X Bridge C18 column using acetonitrile: ammonium formate in the ratio of (70:30 v/v). The calibration curve was linear from 3.00-700.02 µg/ml for esomeprazole and 0.50-150.08 for NAP, and Mass detection was obtained by ESI/MS/MS in destructive ion mode, checking at m/z 344.19! 194.12, 229.12! 169.05 And 205.13! 161.07 For ESOM, NAP and IS, respectively. The evaluate is suitable for measuring perfect esomeprazole and naproxen plasma concentrations in human bioequivalence study following combined paperwork.[69]

Paul W. Elsinghorst et al. (2011) established a validated sensitive, accurate quantitative liquid chromatography-mass spectroscopy (LC-MS/MS) technique for the purpose of NAP in human plasma was developed and absolutely validated permitting to present FDA and EMA guidelines. The LC-MS/MS scheme is the simultaneous accomplishment of great absolute recovery (90.0±3.6%), the LOD were search to be 0.100_g/mL), high inter-day precision (CV≤9.4%), high analytical recovery (between 94.4 and 103.1%). The linearity range was selected as 0.100–50.0_g/mL (r2 ≥0.998) combined with a short run time of only 2 min.[70]

Capillary electrophoresis (CE) method

Pingping Zhang et al. (2018) Investigation of capillary electrophoresis coupling with chemiluminescence recognition scheme for influential naproxen was developed based on the improved chemiluminescence concentration of the luminol and K3Fe(CN)6 in alkaline solution. The disjunction was conducted in 30 m mol L-1 borate buffers at pH 10.0. The linearity range was selected as 10-2000 µg/ml, and LOD and LOQ was found to be 2.7 µg L−1 and 8.8 µg L−1, respectively. The proposed method was useful to identify NAP in human urine sample with acceptable analyse results.[71]

Potentiometric methods

Ulku Dilek Uysal et al. (2004) This paper designates the potentiometric method to quantify naproxen in tablets. The solvent system composition of aqueous solution of 20% ethanol with an ionic capacity of 0.1 additional sodium chloride has been discover to be appropriate for naproxen examination. Similar solvent system was employed for titrant of 0.1 N HCl and to titrate the active material. Validation processes as repeatability (precision) (n=6) were calculated. It was found to be 0.70 for RSD% and 0.3 for ±CL (p=0.05). The analysis of 275 and 550 mg naproxen sodium tablets was carried out in the filtered and unfiltered tablet solutions for three successive days considering intra and inter-days. Precision values were in the range of 0.16-0.33 for unfiltered and 0.10-0.29 for filtered solutions and the amount of the tablets was found to be in the range of (103.0-108.7%) for unfiltered and (102.9-107.7%) for filtered solutions. The method proposed here is precise simple and rather cheap. Therefore, it is suggested for the routine analysis of naproxen sodium tablets.[72]

Conclusion

The present review illustrates different analytical approaches exercised for the assessment of NAP. A frequent investigation had present including, Bio-analytical, HPLC, HPTLC, UV/Vis-Spectroscopy, Spectrofluorimetry, capillary electrophoresis, LC-MS, LC-ESI-MS etc. for estimation of NAP in bulk and in its combined pharmaceutical formulations and in plasma. Liquid chromatography with UV detection has been found to be most studied for estimation of NAP in bulk and pharmaceutical dosage forms, while hyphenated LS-MS, LS-MS/MS methods are reported for determination of NAP and its metabolite in plasma and other biological fluids. Further, methods were reported for its pharmacokinetic and bioequivalence studies. Few chromatography approaches like HPTLC and Stability-indicating HPLC and HPTLC are also reported in literature. Definite Spectrophometric methods in UV-Visible along with fluorimetric are mainly often used for estimation for NAP.

Abbreviations

NAP- Naproxen; **ESOM**-Esomeprazole; **DOM**-Domperidone; **PARA**-Paracetamol; **PAN**-Pantoprazole; **RAN**-Ranitidine; **SUMA**-Sumatriptan; **λmax**-Wavelength Maxima; **LIN**-Linearity; **FR**-Flow Rate; **RT**-Retention Time; **RF**-Retention Factor; **UV-VIS**- UV/Visible Spectrophotometry; **HPLC**- High Performance Liquid Chromatography; **RP-HPLC**- Reverse Phase Liquid Chromatography; **HPTLC**- High Performance Thin Layer Chromatography; **LC-MS/MS**- Liquid Chromatography Mass Spectrometry/Mass Spectrometry; **UPLC-MS/MS**-Ultra Pressure Liquid Chromatography-Mass Spectrometry-Mass Spectrometry; **ODS**- Octadecyl silane; **OPA**-Orthophosphoric Acid; **IUPAC**- International Union of Pure and Applied Chemistry; **IP**-Indian Pharmacopoeia; **Cm**-Centimetre; **mm**-Millimetre; **nm**- Nanometre; **µL**- Micro

Litter; **µg**-Microgram; **REF**- Reference; **DMF**-Dimethylformamide; **NaOH**-Sodium Hydroxide; **KOH**-Potassium Hydroxide; **ACN**-Acetonitrile; **MeOH**-Methanol; **EtOH**-Ethanol; **GAA** –Glacial Acetic Acid; **LOD –** Limit of Detection; **LOQ –** Limit of Quantification.

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