REVIEW ARTICLE

A Review on Different Analytical Techniquesfor the Estimation of Tapentadol

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ABSTRACT

Tapentadol is a hydrochloride of 3-[(1R,2R)-3-(dimethyl amino)-1-ethyl-2-methylpro-pyl] phenol. Tapentadol being an artificial new painkiller that operates as an opioid receptor agonist and a noradrenaline re-uptake inhibitor in the central nervous system. Tapentadol glucuronide conjugate is a significant breakdown product expelled in urine, and unsettled stomach and nausea are common side effects. This review article explains the estimation of tapentadol and related compounds using instruments such as UV-visible spectrophotometer, capillary electrophoresis, high-performance thin-layer chromatography (HPTLC), high performance liquid chromatography (HPLC), liquid chromatography with tandem mass spectrometry (LC-MS-MS), ultraperformance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). In addition, this review summarizes tapentadol's pharmacodynamics, pharmacokinetics, and drug interactions.

Keywords: HPLC, LC-MS, Opiod analgesic, Tapentadol.

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INTRODUCTION

Pharmaceutical analysis is typically described as analytical chemistry that deals with pharmaceuticals in both their bulk and finished forms.[1] In general, this refers to the use of a method to identify a medication (single or combination) in its bulk or pharmaceutical dosage form. Chemical, physical, and sometimes microbiological analyses are used to test pharmaceutical products. There are two sorts of methodologies for pharmaceutical analysis. Qualitative approaches are commonly employed to determine the existence or identification of a component or contaminants. Quantitative approaches are used to determine the amount of known medications in bulk or in a formulation.[2]

Tapentadol is a centrally acting pain reliever with a two-fold mode of act that provides analgesic efficacy comparable to that of a pure mu-opioid receptor agonist but with a better side effect profile. Tapentadol (3-((1R,2R)-3-(dimethyl amino)-1-ethyl-2-methylpropyl) phenol hydrochloride) is a non-racemic molecule. Tapentadol's molecular formula is $C_{14}H_{23}NO.HCl$. Pain is an illness that affects every person and is notoriously hard to treat. NSAIDs, opioids, and paracetamol are among the current drug treatment choices for pain control. Because of the ceiling effect, NSAIDs are only effective for modest to moderate pain alleviation. Patients with renal weakness, acid peptic disease or a tendency to hemorrhage should avoid taking NSAIDs.[3]

Pharmacodynamics

Tapentadol is a non-natural painkiller that performs as a Micro-Opioid Receptor (MOR) agonist and inhibits noradrenaline re-uptake. Through mu-opioid agonistic action, it changes sensory and emotional elements of pain, slows pain transmission at the spinal cord, and disturbs pain perception-action. It causes analgesia by increasing the amount of noradrenaline in the brain by preventing its re-absorption into nerve cells at central nervous system (CNS) sites.[3,4]

Pharmacokinetics

Oral administration of TAP results in a 32% absorption rate. Gastric pH or gastrointestinal motility had no effect on its pharmacokinetics, and it could be taken with or without food.[5] It is broadly spread all over the body and does not require metabolic initiation to function. Tapentadol enantiomer penetrates the blood-brain barrier quickly and has a quick beginning of action. Tapentadol's maximum concentration and area under curve values amplified at 50–150 mg dosage, and plasma-protein binding was roughly twenty percent. After oral administration, the plasma $t_{1/2}$ is approximately 4 hours, and the greatest effect is achieved after 1-hour, with a period of action of 4–6 hours.[3]

Drug Interactions

Because tapentadol has a poor affinity for proteins, dislocation reactions are uncommon. Tapentadol has a little risk of drug-

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drug interactions due to its pharmacokinetic properties. When tapentadol was combined with naproxen, aspirin or paracetamol, no significant changes in plasma concentration were found. Tapentadol and metoclopramide, as well as omeprazole and probenecid, have no pharmacological interactions. Additional opioids, phenothiazines, sedative-hypnotics, general anesthetics, or other central nervous system depressants like alcohol may cause further central nervous system depression, which might present as hypotension, hypoventilation, or deep drowsiness in patients using tapentadol.

UV-VIS SPECTROPHOTOMETRIC METHOD

The quantitative measuring of a material's reflection or transmission qualities as a function of wavelength is known as spectrophotometry. These approaches have the advantage of requiring little time and effort. These approaches have good precision as well. Over the previous years, the application of UV–visible spectrophotometry, particularly in investigating therapeutic dosage forms, has expanded.[30] The quantitative measurement of tapentadol using UV-vis spectrophotometric methods is listed in Table 1.

Jain D and Basniwal PK[4] used a linear regression equation approach to design and validate a modest, exact, and subtle ultraviolet spectrophotometric way to measure tapentadol hydrochloride in the tablet dosage form. The absorbance of tapentadol hydrochloride was measured at 272 nm. Linearity was detected in concentration ranges of 10 to 50 µg/mL, with R^2 value of 0.9990. The projected process is cost-effective, accurate, specific, and subtle for the assessment of tapentadol in its formulation and bulk drug.

A study by Patil. *et al*.[5] have established a unique, simple, sensitive, and quick spectrophotometric approach for the quantification of tapentadol HCl. The linearity of tapentadol HCl in water and 0.1N hydrochloric acid was determined. The range was found to be 5-30g/mL, with R^2 of 0.9981 and 0.9996. From the water, the average recovery percentage was 99.32%, and from 0.1N hydrochloric acid, it was 99.99%. The devised spectrophotometric approach was simple, linear, environmentally friendly, detailed, and true, and it could be used for repetitive quality control investigation of tapentadol hydrochloride in tablet form.

Babu. *et al*.[6] developed a modest, inexpensive, detailed, dependable, and reproducible visible spectrophotometric technique for the assessment of tapentadol in bulk along with tablet formulations. This process is grounded on developing blood-red colored chromogen with 1,10 phenanthroline, which displays extreme absorption at 510nm. Over the range of 10-100g/ml, the concentration plot is linear. The results of the analysis were statistically corroborated. Studies on recovery have also been done. The suggested approach is cost-effective, precise, and sensitive for the estimation of tapentadol in bulk medication and its formulation.

Mobrouk. *et al*.[7] devised two modest, rapid, environmentally friendly, and dependable spectrophotometric techniques for assessing tapentadol hydrochloride in bulk and artificial mixtures comprising probable excipients. The first method involves measuring the drug's aqueous solution's first derivative values at 228 nm, while the second method involves assessing the 2nd derivative values at 235 nm. Calibration graphs created at their wavelengths of determination for both methods in the concentration array of tapentadol 5- 60 g.ml-1 were linear. The proposed methodologies have undergone comprehensive validation in accordance with ICH recommendations. The spectrophotometric procedures described in this work are modest, true, detailed, exact, and repeatable and can be used straight in pharmaceutical dosage forms.

Krishnamoorthy *et al*.[8] established and validated in his study a simple and repeatable UV spectrophotometric technique for the quantifiable measurement of tapentadol HCl

Table 1: Determination of tapentadol by UV-Visible spectrophotometer

S. No	*Drug*	*Instrument*	*λ max(nm)*	*Parameters*	*References*
1	Tapentadol Hcl	UV spectrophotometer	272	Linearity, accuracy, precision, repeatability, robustness	4
2	Tapentadol hydrochloride	UV spectrophotometer	214	Linearity, LOD, LOQ, accuracy, precision	5
3	Tapentadol hydrochloride	UV spectrophotometer	275	Linearity, precision, recovery, stability studies	6
4	Tapentadol hydrochloride	UV–vis spectrophotometer	First derivative absorbance (1D) at 228 Second derivative absorbance (2D) at 235	Linearity, accuracy, precision, specificity	7
5	Tapentadol hydrochloride	UV spectrophotometer	271	Linearity, accuracy	8
6	Tapentadol	Ultra violet- Visible double beam spectrophotometer	510	Molar absorptivity, sandells sensitivity, precision	9
7	Tapentadol hydrochloride	UV/vis double beam spectrophotometer	272	Linearity, accuracy, precision, specificity, robustness	10
8	Tapentadol hydrochloride	UV/vis double beam spectrophotometer	750	Linearity, accuracy, precision, specificity, robustness	10

in bulk and dosage form. The maximal wavelength of tapentadol hydrochloride is 271nm. Beer's law was followed with a R^2 of 0.9996 in the concentration range of 42.85–61.15 g/mL. Recovery trials for Tapentadol hydrochloride were conducted, and percentage recovery was found to be in the 99.95% range, verifying the accuracy of the suggested approach. The new approach demonstrated good reproducibility and recovery with a percent RSD of less than two. The projected technique can be effectively employed for the repetitive assessment of tapentadol HCl in pure and pharmaceutical tablet formulations, according to statistical validation of the data.

Vanitha Prakash. *et al*.[9] devised a simple, inexpensive, exact, reliable, and repeatable spectrophotometric approach for the measurement of tapentadol in bulk as well as its formulation. The synthesis of red-colored chromogen, which has a maximal absorption at 510 nm, is the basis for this approach. Over the range of 10–100 g/mL, the absorbance-concentration curve is linear. The outcomes of the study were statistically confirmed. Studies on recovery were also carried out. To estimate tapentadol in bulk medication and its formulation, the suggested approach is cost-effective, precise, and sensitive.

Omkar *et al*.[10] devised and verified three simple, accurate, and quick methods for estimating tapentadol hydrochloride in bulk and laboratory tablet samples. At 272 nm, UV-spectrophotometric analysis of tapentadol was performed. According to ICH criteria, the devised procedure was validated. The proposed way is cost-effective, accurate, detailed and subtle for the assessment of tapentadol in bulk drug and its dosage form.

Omkar *et al*.[10] devised and verified three new, simple, accurate, and quick methods for estimating tapentadol HCl in bulk and laboratory tablet samples. The Folin-Ciocalteu reagent is used to measure tapentadol in the presence of a 20% sodium carbonate solution in this method. Tapentadol's blue color chromogen is evaluated against a reagent blank at a wavelength of maximum absorption of 750 nm. According to ICH criteria, devised procedure was validated. The projected technique is cost-effective, true, specific, and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

CAPILLARY ELECTROPHORESIS

Capillary electrophoresis is an important device used in pharmaceutical analysis. Capillary electrophoresis is a comparatively new diagnostic method that involves the parting of charged analytes using a tiny capillary and an electric field. As solutes flow through the detector, they are recognized as peaks, and the area of each peak is relative to their concentration, allowing quantitative calculations. It is used in the examination of biopolymer study and inorganic ions, in addition to pharmaceutical investigations. Capillary electrophoresis analysis is normally more operative, can be accomplished in a shorter length of time, wants just a minor volume of material, requires smaller injection volumes (up to Nano litres), and takes place in most situations under aqueous conditions[30]. Table 2 shows the quantitative measurement of tapentadol using the capillary electrophoresis (CE) method.

Znaleziona *et al*.[11] used capillary electrophoresis to investigate the chiral acknowledgment of the centrally acting pain reliever tapentadol and its isomers with several cyclodextrins, with a focus on the relocation directive of 4 stereoisomers. In the instance of uncharged hydroxy propylated CDs, the β derivative was able to separate the S, R- and R, S-isomers in an acidic related electrolyte, whilst the γ permitted the parting of S, S- and R, R-tapentadol, respectively. A double cyclodextrin system with both hosts was used to detach all four isomers. The optimised technique could regulate 0.15% of chiral impurities of tapentadol in the occurrence of the last wandering clinically relevant R, R-isomer using negatively charged sulphated—cyclodextrin at one percent (w/v) concentration in 100 mM sodium borate buffer (pH 9.5). The planned process is inexpensive, exact, detailed, and subtle for the assessment of tapentadol in bulk drugs and its formulation.

HIGH-PERFORMANCE THIN-LAYER CHROMATOGRAPHY (HPTLC)

HPTLC has become an important tool in drug analysis as technology has progressed. HPTLC is a quick separation method that may be used to analyze a wide range of materials. This technique is obliging in many ways, counting its ease of usage and the fact that it just takes a short amount of period to analyze the complex sample clean-up. HPTLC estimates the full chromatogram in real-time using a range of factors. Furthermore, numerous samples and standards are developed simultaneously yet independently on each plate, resulting in greater results reliability[30]. The quantitative measurement of tapentadol using HPTLC methods is listed in Table 3.

Kathirvel and Madhu Babu[12] determined a modest HPTLC technique for tapentadol HCl in bulk and its formulation. The medication was parted on aluminum plates precoated with silica gel and a mobile phase of 6:2:2 (v/v/v) butanol: water: glacial acetic acid. Densitometric scanning at 254 nm was used for quantitative analysis. The method's linearity, accuracy, precision, and robustness were all tested. The calibration plot was linear over the 200–600 ng band -1 range for tapentadol hydrochloride. The procedure was used to analyze a medication in a pharmaceutical dose form and was found to be effective.

Roy *et al*.[13] created and evaluated a modest, accurate HPTLC technique for estimating tapentadol HCl in tablet dosage form. The mobile phase was chloroform: acetone: ammonia (2.5: 2.4: 0.1 v/v/v), and the chromatography was done on silica gel plates. Tapentadol hydrochloride was resolved

Table 2: Determination of tapentadol by capillary electrophoresis

S. No	*Drug*	*Instrument*	*Stationary phase*	*Parameters*	*References*
1	Tapentadol	Capillary electrophoresis	Micro Solv, 50 µm i.d.,365 µm o.d., total capillary length 64.5 cm	LoD, LoQ, recovery	11

well using this mobile phase technique. At 272 nm, findings and estimation were performed. The calibration plot's linear regression data indicated a decent association with r = 0.999. Tapentadol hydrochloride had LoQ and LoD of 189.94 and 62.68 ng/spot, respectively.

Amin *et al*.[14] devised a modest, true, quick, and subtle HPTLC technique for the measurement of tapentadol HCl in bulk and its dosage form. The medicines were parted by chromatography on aluminum plates precoated with silica gel as the stationary phase and methanol: toluene (4:1v/v) solvent solution. The divided zones were densitometrically evaluated by means of an UV detector set to 272 nm. The drug was determined adequately with an R_f value of 0.5 0.02. Over a concentration range of 1500 to 2000 (1.–2.0 L) ng/spot, the technique was linear. It was discovered that the analytical percent recovery was 99.92%. With percent relative standard deviation values extending from 0.0895 to 0.0892, the intraday and interday precision range from 0.0895 to 0.0892. The approach was legalized in accordance with ICH guidelines. The proposed HPTLC approach was successfully used to analyze bulk medication and its commercial tablet dosage form regularly.

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

High performance/pressure liquid chromatography is a sort of liquid chromatography used to separate complicated mixtures of molecules found in biological and chemical systems to understand the roles of discrete components. The HPLC method has great selectivity and may achieve appropriate precision simultaneously. The pharmaceutical sector relies heavily on HPLC to address a variety of queries[30]. The quantitative measurement of tapentadol using HPLC methods is listed in Table 4.

Ishaq. *et al*.[15] demonstrated a method whose linearity was demonstrated for both tapentadol and tramadol, tapentadol and tramadol had R^2 values over 0.99. The LLoQ for tapentadol was found to be 9.775 ng/mL, while upper limit of quantification was determined to be 5024.376 ng/mL. HPLCePDA experiments indicated that the chromatographic runs were selective, with no intrusive peaks during the retention periods of the analyte (tapentadol) and ARE (tramadol). The planned process is inexpensive, true, detailed, and subtle for the assessment of tapentadol in bulk drug and its dosage form.

Table 3: Determination of tapentadol by HPTLC

S. No	*Drug*	*Instrument*	*Mobile Phase*	*Parameters*	*References*
1	Tapentadol hydrochloride	HPTLC	Butanol: water: glacial acetic acid 6:2:2 (v/v/v)	Linearity, accuracy, precision, specificity, LOD, LOQ	12
2	Tapentadol hydrochloride	HPTLC	Chloroform: Acetone: Ammonia (2.5: 2.4: 0.1 v/v/v)	Linearity, LOD, LOQ, accuracy, precision, assay	13
3	Tapentadol hydrochloride	HPTLC	Methanol: Toluene (4:1v/v)	Linearity, precision, accuracy, robustness, specificity	14

Table 4: Determination of tapentadol by HPLC

S. No	*Drug*	*Instrument*	*Mobile Phase*	*Stationary Phase*	*Parameters*	*Reference*
1	Tapentadol	HPLC	0.1 M Dipotassium Phosphate buffer and acetonitrile in the ratio of50:50 %v/v	Water'sXterra C8 (150 mm×4.6 mm, 5mm)	Linearity, recovery, accuracy, precision, LOD, LOQ, stability studies	15
2	Tapentadol hydrochloride	RP-HPLC	0.1 mM Dipotassium Phosphate buffer	C18 Licrosphere column (150 mm4.6 mm inner diameter,5mm particle size)	Linearity, accuracy, precision, LoD, LoQ, ruggedness, robustness	16
3	Tapentadol	HPLC	Heptane–propan-2-ol– di ethyl amine (980:20:1, v/v/v)	Chiral Pak AD-H	Linearity, accuracy, precision, LoD, LoQ	17
4	Tapentadol	HPLC	Acetonitrile: acetic acid	SunFireTM C18 (150 mm × 4.6 mm inner diameter, 5 m particle size)	Linearity, accuracy, LoD, LoQ, stability studies, robustness	18
5	Tapentadol	HPLC	Acetonitrile: acetic acid	SunFireTM C18 (150 mm × 4.6 mm inner diameter, 5 m particle size)	Concentration	[19]
6	Tapentadol hydrochloride	HPLC	Methanol: water (60:40 v/v)	Chromasil C18 (4.6 x 250 mm, 5 µm	Linearity, sensitivity, selectivity, accuracy, precision, LoD, LoQ, stability studies	20
7	Tapentadol hydrochloride	HPLC	50 mM phosphate buffer pH 3.62: acetonitrile 70:30 (% v/v)	HiQ Sil C8 column 250 x 4.6 mm and 5µm	Linearity, accuracy, precision, specificity, robustness	10

Muziba. *et al*.[16] devised a method for tapentadol hydrochloride, which has a linear calibration curve from 75 to 450 mg/mL. A total of 0.9994 was discovered to be the correlation coefficient (r 2) value. According to the precision research, the %CV value was less than 2% in all specified concentrations. Tapentadol hydrochloride has a percent recovery rate between 99.96 and 100.01%. Tapentadol hydrochloride has a LoD and a LoQ of 0.25 and 0.75 mg/mL, respectively. The projected process is cheap, true, detailed and subtle for the assessment of tapentadol in bulk drug and its dosage form.

Douša *et al*.[17] devised and verified a sensitive and explicit HPLC approach for the parting and assessment of tapentadol enantiomers. On Chiral Pak AD-H, excellent enantio separation was accomplished with a resolution of more than 2.5 for all enantiomers using a blend of heptane-propan-2-ol-diethylamine (980:20:1, v/v/v). The exposure was done utilizing a fluorescence detector with a 295 nm excitation wavelength and a 273 nm emission wavelength. The developed technique was validated using the ICH requirements for LoD, LoQ, precision, accuracy, linearity, and selectivity. The method's advantages include good enantio separation and a fast analysis time (less than 20 minutes), making it appropriate for routine chiral purity testing of (R, R)-tapentadol in an enantiopure active pharmaceutical component.

Giorgi *et al*.[18] tested the method's applicability by giving TAP to 2 dogs orally; the technique produced predictable pharmacokinetic results, with plasma taken at regular intervals through jugular venipuncture. The mobile phase was acetonitrile (A): acetic acid (B) given in gradient mode. Tapentadol was mined from plasma using a diethyl ether: dichloromethane (7:3, v/v) mixture that yielded a recovery of 98.0-107.8% and a quantification limit of 1-ng/mL1. In conclusion, utilizing HPLC-FL to sense tapentadol in plasma was a straightforward and effective method that could benefit future pharmacokinetic research.

Lavy *et al*.[19] quantified the concentrations of tapentadol in plasma using a legalized HPLC method. The projected process is reasonable, true, detailed, and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

Sonali Mahaparale and Nikita Samuel[20] developed and validated a a modest, quick, selective, subtle, accurate, and precise HPLC with UV detection technique for the analysis of tapentadol hydrochloride in human plasma. Tapentadol HCl was separated chromatographically by means of a chromasil C18 column and a mobile phase of water: methanol (40:60 v/v) at a flow rate of 1.0 ml/min. To extract medication from plasma samples, acetonitrile was used as a precipitating agent. Tapentadol HCl linearity was assessed to be 100-1000 ng/ml, with a r^2 of 0.9980. The technique has been used to achieve pharmacokinetic and bioequivalence studies in human plasma.

Omkar *et al*.[10] devised and tested three new, simple, accurate, and quick procedures for valuing tapentadol hydrochloride in bulk and tablet samples. Elution was obtained in isocratic mode using a mixture of 50 mM phosphate buffer with a pH 3.62 and acetonitrile in a 70:30 (%v/v) ratio with 0.1% triethylamine and a HiQ Sil C8 column with a specification of 250 x 4.6 mm and 5 m particle size in the RP-HPLC method. The detection was done at 285 nm, and the flow rate was 1-mL/min. The projected process is cost-effective, true, specific, and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY (LC–MS)

One of the greatest events of the previous era of the twentieth century is liquid chromatography with mass spectrometry. It became the technique of choice for analytical sustenance in several pharmaceutical quality control and assurance stages. Its use in drug analysis HPLC has been used to analyze pharmaceutical contaminants and degradation products both alone and in combination with hyphenated techniques.[30] The quantitative measurement of tapentadol using LCMS methods is listed in Table 5.

Howard *et al*.[21] established and confirmed a highly subtle and quick LC–MS–MS method. After oral dosing, tapentadol was readily absorbed. After tapentadol injection at 10, 20, and 30 mg/kg, the geometric mean terminal plasma half-life was 3.5 hours, 3.7 hours, and 3.7 hours, respectively. All dogs had tapentadol and its three measured metabolites, which accounted for 0.16 percent, 2.8, 97, and 0.04% of the overall area beneath the concentration-time curve, respectively. The planned technique is cheap, true, detailed, and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

Tzschentke *et al*.[22] injected drugs intraperitoneally in isoflurane-anesthetized mice and samples were collected for 3 hours before being assessed for monoamine content with the help of HPLC-MS/MS. Tapentadol showed a dose-dependent, substantial rise in extracellular spinal norepinephrine levels in standings of area-under-curve. A total of 60 minutes after receiving 10 mg/kg tapentadol, a maximum rise of 18.232% over baseline was achieved. Venlafaxine (10mg/kg) had a similar level of effect. The anticipated technique is cost-effective, true, detailed and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

Jones and Handy[23] established and legalized a highly subtle and quick LC–MS–MS method. Whole blood calibrations from 0.025 mg/L to 5.0 mg/L and separately generated whole blood controls 0.5 mg/L were used to determine percent accuracy. In post-mortem case blood (n 14 10) recovery spikes averaged 96.2% at 0.075 mg/L and 100.1% at 4.0 mg/L. The projected technique is cheap, accurate, detailed, and subtle for the assessment of tapentadol in bulk drug and its dosage form.

Wu. F *et al*.[24] designed and validated a high throughput LC–MS–MS method. Methylphenidate had the greatest positive rate in urine specimens, followed by tramadol, fentanyl, tapentadol and meperidine. Both parent drug and its breakdown products were detectable in 94.9% of meperidine models, 94.5% of tramadol models, 93.8% of fentanyl tests, and 89.9% of methylphenidate, and 86.6% of tapentadol models.

Table 5: Determination of tapentadol by LC-MS/MS

S. No	*Drug*	*Instrument*	*Mobile Phase*	*Stationary phase*	*Parameters*	*References*
1	Tapentadol Hydrochloride	HPLC-MS/MS	0.1% formic acid in water (solvent A) and 0.1% formic acid in acetonitrile (solvent B)	Column (2.1 mm X 50 mm X 1.8 µm)	Concentration	21
2	Tapentadol	HPLC-MS/MS	UP/ACN (98/2) 0.1% FA (mobile phase A) and UP/ACN 0.1% FA (30/70) (mobile phase B)	Reversed-phase Phenomenex Synergi MAX-RP 100 mm × 3.0 mm (2.5 m particle size)	Concentration	22
3	Tapentadol	LC-MS/MS	Mobile phase A: 0.1% v/v formic acid in deionized water. Add 1 mL of formic acid to a 1 L graduated cylinder. Fill to volume with deionized water and mix. Mobile phase B: acetonitrile.	Agilent Poroshell SB-C18, 2.1 × 100 mm, 2.7 µm	Accuracy	23
4	Tapentadol	LC-MS/MS		C18 UPLC analytical column (2.1×50 mm, 1.8µm particle size, Waters) and BEH C18 UPLC column (2.1×50 mm, 1.8µm particle size, Waters)	Assay	24
5	Tapentadol	LC–MS/MS	20 mM ammonium formate (pH 6.4) (Sol-vent A) and methanol (Solvent B) (85:15)	Zorba Eclipse XDB C18 (4.6×50 mm×1.8 mm)	Linearity, sensitivity, selectivity, accuracy, precision	25
6	Tapentadol	LC–MS/MS	Methanol and 5 mmol·L (-1) ammonium acetate（0.01% ammonia)	XDB C (18) 50 mm × 4.6 mm, 1.8 µm） column	Linearity, precision, accuracy	26

The data shows the metabolic trends of five pharmaceuticals in people who have been administered these prescriptions, based on a random urine or serum/plasma sample.

Coulter *et al*.[25] used LC-MS/MS as an analytical approach for determining the novel pain medicine tapentadol and its major breakdown product N-desmethyltapentadol in urine and oral fluid has been devised and legalized (LC-MS-MS). QuantisalTM devices were used to collect oral fluid, and medications were measured using SPE and LC with tandem mass spectral detection. The quantifying transition for tapentadol was 222.1 > 107, and the qualifier was 222.1 > 121. The linear range for saliva was 10 to 100 ng/mL; intraday precision was 3.6%, interday precision was 13.6%, and intraday precision was 3.6% (n = 6). Tapentadol and DMT were recovered in greater than 99% of cases from the oral fluid collecting pad. This is the first time tapentadol and DMT have been detected in urine and mouth fluid.

Liang *et al*.[26] used LC-MS/MS to establish a simple and rapid process for determining tapentadol in dog plasma and to assess the impact of conjugated metabolites on tapentadol quantification. The analyte and tramadol (IS) were mined from plasma by protein precipitation with methanol and chromatographed on an XDB C (18) (50 mm 4.6 mm, 1.8 m) column with methanol as the mobile phase and 5 mmolL (-1) ammonium acetate as the stationary phase (0.01 percent ammonia). Tapentadol standard curves were found to be linear in the range of 0.100–20.0 ngm L (-1). Precisions were within 5.1% intra- and inter-day, with accuracy ranging from -3.2% to 0. The pharmacokinetics of tapentadol hydrochloride sustained release tablets in Beagle dogs were successfully studied using this method.

ULTRA-HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (UHPLC)

The term "ultra-high-performance liquid chromatography" refers to liquid chromatography separations that use columns that encapsulate particles lesser than the 2.5 to 5 m size range commonly used in HPLC. UHPLC works on the same premise as HPLC, with the controlling principle that efficiency and resolution increase as column packing particle size decreases. UHPLC provides the entire assistance of chromatography submissions for separations using shorter columns, superior flow rates for augmented quickness, and greater resolution and sensitivity in today's world[31]. The quantitative measurement of tapentadol using UPLC–MS methods is listed in Table 6.

Hillewaert *et al*.[27] designed and validated a high throughput UPLC-MS/MS assay to quantify tapentadol and its O-glucuronide breakdown product in human serum. Tapentadol took 1.6 minutes to run while tapentadol-O-glucuronide took 1.5 minutes. The assay's excellent sensitivity and good performance allowed it to be used in clinical trials to analyse serum samples. Over 17,000 samples of tapentadol were analyzed using the validated method.

Liu *et al*.[28] established and authorized an extremely subtle and quick UPLC-MS/MS technique for concurrently detecting

Table 6: Determination of tapentadol by UPLC-MS/MS

S. No	*Drug*	*Instrument*	*Mobile Phase*	*Stationary phase*	*Parameters*	*References*
1	Tapentadol and Tapentadol-o-glucuronide	UPLC–MS/MS	ACN (A):0.2% acetic acid (B)	SunFireTM C18 analytical column (150 mm × 4.6 mm inner diameter, 5 m particle size, Waters, Dublin, Ireland)	Linearity, accuracy, precision, LoD, specificity, stability studies	27
2	Tapentadol and its carbamate prodrug	UPLC-MS/MS	Methanol (A) and water (B)	Phenomenex Kinetex® XB-C18 (2.1 mm × 50 mm × 2.6 µm)	Linearity, accuracy, precision,	28
3	Tapentadol and N-Desmethyl tapentadol	UPLC-MS/MS	0.1% formic acid (Solvent A) and acetonitrile (Solvent B)	Waters Acquity UPLC® BEH Shield RP18 (2.1 mm × 50 mm × 1.7 µm)	Linearity, accuracy, precision, sensitivity, selectivity	29

tapentadol and WWJ01 in rat plasma using fluconazole as an internal reference. Methanol was used to treat the analytes and internal standard, which were then parted on a Phenomenex Kinetex® XB-C18 (2.1 50 mm 2.6 m) column at a flow rate of 0.3 mL/min. Methanol and water made up the mobile phase, which was eluted in a gradient. Excellent linearity was reported for both tapentadol and WWJ01 over the concentration range of 2–1250 ng/mL (r = 0.995), with a lower limit of quantification of 2 ng/mL. The validated method was true, rapid, and repeatable and effectively applied to pharmacokinetic studies of tapentadol and WWJ01.

Bourland *et al*.[29] devised a technique for both tapentadol and N-desmethyl tapentadol. The method's linearity was established with R^2 above 0.99 and linear ranges of 50 to 500,000 ng/mL for tapentadol and 100 to 500,000 ng/mL for N-desmethyl tapentadol. The assay's intraday precision for both analytes was from 2.2 to 6.9% over 3 concentrations, whereas the interday precision for both analytes was 1.2 to 8.4%. Tapentadol and N-desmethyl tapentadol had quantitation limits of 50 and 100 ng/mL, respectively, while the upper limit of linearity for both analytes was discovered to be 500,000 ng/mL. The projected way is cost-effective, true, detailed and subtle for the assessment of tapentadol in bulk drugs and its dosage form.

CONCLUSION

Tapentadol (R, R–form) is a new opioid pain reliever with a twin mechanism of action for sensible to unadorned acute pain. Different analytical methods such as UV, HPLC, HPTLC and hyphenated techniques such as UPLC-MS/MS, LC-MS/MS methods were reported for the estimation of tapentadol in bulk, pharmaceutical dosage forms, and biological samples. Among these techniques, LC-MS-MS, UPLC-MS-MS showed good results due to their greater resolution and sensitivity. In addition, there are a greater number of HPLC techniques for the assessment of tapentadol in bulk and pharmaceutical dosage forms. The present study offers a short overview of analytical procedures for the assessment of tapentadol in pharmaceutical formulations and biological specimens.

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