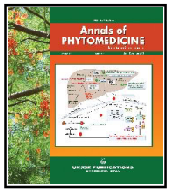
Annals of Phytomedicine 12(2): 299-303, 2023

DOI: http://dx.doi.org/10.54085/ap.2023.12.2.37

Annals of Phytomedicine: An International Journal

http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

An overview of analytical methods for quantification of paracetamol

R. Gandhimathi◆, V. Nivathra, and C. M. R. Kajhareshevarmaa

Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology, and Advanced Studies (VISTAS), Pallavaram-600117, Chennai, Tamil Nadu, India

Article Info

Article history

Received 13 November 2023

Revised 24 December 2023

Accepted 25 December 2023

Published Online 30 December 2023

Keywords

Acetaminophen

Prostaglandin

Acetanilide

Spectrophotometric

Flow rate

Abstract

Both the international names paracetamol (used in Europe) and acetaminophen (used in the United States) are official names in the case of the same chemical substance. In an attempt to exterminate worms in the 1880s, two teenage physicians acetanilide was administered to a patient at the University of Strasburg accidentally in place of naphthalene. They observed that even though the drug greatly lowered high fever, it possessed very little impact on intestinal parasites. After a year, Frederick Stearns and Co., a division of Sterling Drug Inc., started offering 500 mg of aspirin pills over the counter in Great Britain under the brand name panadol. A spectrophotometric approach based on continuous flow for detecting paracetamol in pharmaceuticals is described. Created a stability-indicating technique to use the TLC densitometry method to figure out how much paracetamol is in pharmaceutical preparations. An effective approach for detecting acetaminophen in pharmaceutical formulations using reverse-phase high-performance liquid chromatography was developed. At a flow rate of 1.78 ml/min, a combination of methanol and water (1:2 v/v) is employed with a C18 stationary phase, with spectrophotometric detection 193.3 nm. Created a method for determining paracetamol using differential pulse voltammetry at a carbon ionic liquid electrode. A carbon paste electrode (CPE) and carbon ionic liquid electrode (CILE) were both used to study how paracetamol behaves electrochemically in a 0.1 m acetate buffer solution (pH 4.6). For example, long-term alcohol abuse combined with concurrent usage of medications that cause enzyme induction, including barbiturates, or carbamazepine, could make paracetamol poisoning more likely.

1. Introduction

Both the terms paracetamol (an international name used in Europe) and acetaminophen (an international name used in the United States) are interchangeable official names for the identical chemical, which is taken from its chemical name: N-acetyl-para-aminophenol. This drug has a long history of use and was discovered by chance, as important discoveries frequently do (Sumithra, 2023).

In an attempt to exterminate worms in the 1880s, two youthful physicians acetanilide was administered to a patient at the University of Strasburg accidentally instead of naphthalene. They observed that even though the drug greatly lowered high fever, it possessed very minimal impact on parasitic intestinal worms. Following the prompt publication of their findings by two young physicians, Arnold Chan and Paul Heppa, acetanilide was first used in medicine in 1886, by the trade appellation antifebrin. It shortly became clear that despite its low cost of production, it was not possible to use acetanilide because of its antipyretic properties, the majority concerning among which methemoglobinemia was one. That led to extensive research on less poisonous acetanilide derivatives. The most pleasing chemicals were phenol and N-acetyl-p-aminophenol, which were previously produced in 1878 by Harmon Northrop Morse (Subhamalar *et al.,* 2023).

Joseph von Mering, a pharmacologist from Germany conducted two acetanilide derivatives' initial clinical trials. Based on the data, it was incorrectly concluded that paracetamol had considerable toxicity, much like acetanilide. As a result, phenacetin was the first derivative to be used in medicine, in 1887. Before its long-term use was linked to nephritis caused by analgesics developing, phenacetin was a common ingredient in analgesic combinations (Vimal Raj and Sumithra, 2023). Paracetamol/acetaminophen gained popularity in 1948, six months later after research by Brodie Bernard and Axelrod Julius showed another metabolite, phenylhydroxylamine, was what caused methemoglobinemia and paracetamol served as the primary analgesic and antipyretic properties of acetanilide and phenacetin's active metabolite.

In 1955, the laboratories of Mcneil brought paracetamol to the pharmaceutical sector as a pediatric prescription marketed as Tylenol children's elixir, an analgesic and antipyretic (the Tylenol comes from N-acetyl-p-aminophenol), the chemical name for it. After a year, the company Frederick Stearns and Co., a division of Sterling Drug Inc., started offering 500 mg of aspirin pills over the counter in Great Britain under the brand name Panadol. Since its introduction into the Polish market in 1961, paracetamol has been one of the most popular and widely prescribed pain reliever drugs. The trade offer includes over 100 products that either contain paracetamol exclusively or in conjunction with additional active ingredients (Raghavi *et al.,* 2023).

Corresponding author: Dr. R Gandhimathi

Professor, Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, Tamil Nadu, India

E-mail: drgmathipharm2017@gmail.com

Tel.: +91-9080766247

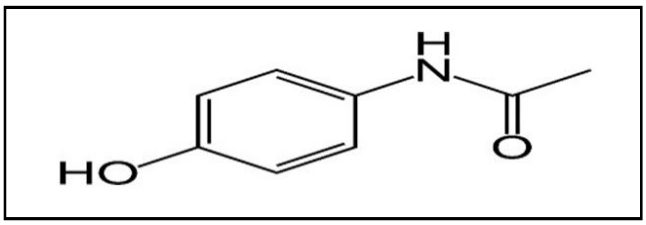


Figure 1: Structure of paracetamol.

2. Dose

The process of paracetamol oxidation, which primarily involves the CYP2E1 enzyme, is minimal in newborns due to CYP2E1 action rises with age, reaching adult levels between the ages of 1 and 10 years (Beauchamp *et al.,* 2013). In contrast, adults' livers mostly metabolize paracetamol through 50-60% glucuronidation, 25-30% sulfation, and less than 10% oxidation (Lee *et al.,* 2016).

3. Pharmacology and recent findings and future directions

3.1 Mechanism of action

Even though the exact manner in which the actions of paracetamol have not been completely elucidated, it is routinely given in addition to nonsteroidal anti-inflammatory drugs because of its ability to block the pathways of cyclooxygenase (COX). Well, it is permissible to use central conduct, which will gradually lead to a decrease in the symptoms of discomfort. A single theory is that paracetamol increases the threshold for discomfort by suppressing prostaglandin production is mediated by two cyclooxygenase isoforms, COX-1 and COX-2. Among prostaglandins, the molecules that cause discomfort sensations. Paracetamol has no effect on cyclooxygenase in supplementary and hence possesses no anti-inflammatory qualities. Although, acetyl-salicylic acid (aspirin) is an unchangeable asset of COX and effectively prevents its action point, research has revealed paracetamol inhibits COX laterally. According to research, paracetamol effectively inhibits an alternative type of the enzyme, which differs from the recognized COX-1 and COX-2 variations. This enzyme is referred to as COX-3. The temperature-regulating activity of acetaminophen is most probably due to focus efforts on temperature regulation centers within the brain, which results in supplemental vasodilation, perspiring, and heat dissipation. The exact medium action of this medicine is not completely recognized at this point, but unborn exploration might lead to a greater understanding (Andersson *et al.,* 2011).

3.2 Pharmacokinetics

Along with peak plasma concentrations occurring between 30 to 60 min of administration and a plasma $t_{1/2}$ of around 120 min, oral paracetamol has high absorption. It diffuses throughout the majority of bodily fluids and binds to plasma proteins less than NSAIDs. Glucuronide conjugates are eliminated *via* the kidneys. When taking a therapeutic dose, 90-100% of the medication is perhaps found in the urine after the initial day. In the main process that converts paracetamol into inert molecules by pairing with glucuronide and sulfate, a small amount is also turned oxidized by an enzyme system called cytochrome P450, which includes the isoenzymes CYP2E1 and CYP1A2. N-acetyl-p-benzoquinone imine is an alkylating metabolite, or paracetamol produces NAPQI when it is converted through the enzymes CYP2E1 and CYP1A2, and it may be this metabolite that causes liver damage. A person's CYP2D6 expression levels can be used to categorize them as extensive, ultra-rapid, or poor metabolizers (Alloui *et al.,* 2002).

3.3 Drug interaction

Co-administration of several medications should be done with caution as there may be interactions with them. For example, long-term alcohol abuse combined with concurrent usage of medications that cause enzyme induction, including barbiturates, or carbamazepine, may increase the likelihood of paracetamol production of NAPQI and toxicity. However, the exact mechanism is unknown due to isoniazid's status as an enzyme inhibitor (Amino Shariae and Khan, 2015).

3.4 Toxicity

While acute overdose of paracetamol is generally safe, it can harm the kidneys, brain, and liver, even leading to death. On rare occasions, even after a therapeutic amount, it causes these effects due to the presence of subclinical risk factors like glutathione deficiency or "fast-metabolizer" status.

Nevertheless, use within the therapeutic range, especially frequent and consistent use, can also have less well-known effects on other organ systems (Ghanem *et al.,* 2016).

3.5 Recent findings and future directions

Abdel Shaheed recently analyzed 36 publications' worth of data and found that while paracetamol was ineffective in other conditions, it did produce minimal alleviation of pain in tension, headaches, arthritis of the hips and knees, as well as pain following a craniotomy. The authors concluded that large-scale, superior trials are necessary to lessen ambiguity regarding the effectiveness of paracetamol in typical pain syndromes (Bannwarth *et al.,* 1992). Recent research has shown that acetaminophen can be safely utilized in those who have chronic kidney illness, that it is significantly effective for pain following arthroplasty, that ibuprofen works better than it does for discomfort following laminectomy, that acetaminophen in emergency room saves opioids, that paracetamol is not advised for pain following lumbar spinal stenosis with neurogenic claudication, and that paracetamol is recommended for pain following postcesarean sections and for migraine (Sridhar Narayan *et al.,* 2009).

Experts should closely evaluate RCTs and other data before implementing the findings in routine clinical practice, or rejecting them. Therapeutic recommendations bridge the knowledge interval between science and practical utilization in medicine. Because they are derived from the consolidated medical data and take into account various financial, factors related to epidemiology, study, and treatment like the accessibility of substitute medical interventions, for instance-they have the advantage of being more thorough. Practice guidelines are, in our opinion, crucial instruments for controlling the intricacy of decision-making procedures (Blyth *et al.,* 2019).

4. Analytical methods for paracetamol

4.1 Spectroscopic techniques

A spectrophotometric determination of paracetamol was developed using iodyl benzene. The spectrophotometric measurement of paracetamol (N- acetyl-4-aminophenol) was performed by oxidizing it in acetone with iodyl benzene to get N-acetyl-1, 4-benzoquino-neimine, a yellow-orange compound, which acquires highest possible

color strength in a 1 min and peaks in absorption at 430 nm. 1.58103 l/mol/cm is the highest molar absorption coefficient (Krishna Verma *et al.,* 1985).

Flow injection and spectrophotometry were used to determine the concentration of paracetamol. The analyte is oxidized alongside potassium hexacyanoferrate and is reacted using phenol. Both responses are conveyed in an aqueous ammoniacal solution at 80°C. The concentrations of paracetamol are measured in the 0.25-30 ppm range (Martinez Calatayud *et al.,* 1986).

A spectrophotometric approach based on continuous flow is described for identifying medicines that contain paracetamol. Reducing paracetamol examples are consistently hydrolyzed in a medium with alkali p-aminophenol that interacts using 3.5 m NaoH and o-cresol using a home microwave oven. The resultant blue derivative exhibits a maximum absorbance of around 620 nm. The threshold for detection of the approach is 0.2 g/ml, the apparatus follows from 0.6 to 20 g/ml, and Beer's law applies (Andres Criado *et al.,* 2000).

The fast technique using spectrophotometry is created to determine acetaminophen. It is predicated upon a 15 min oxidation in 6 m 80°C sulphuric acid and detection around 580 nm (Salah M. Sultan , 1987).

The indirect determination of paracetamol, the luminol-H_2O_2- Fe (CN) 63 system was developed. The method operates by oxidizing paracetamol with hexacyanoferrate (III) and then blocking the luminol-hydrogen peroxide reaction. The method yielded a linear calibration curve with a range of 2.5 to 12.5 g/ml (Gregorio alapont *et al.,* 1999).

An approach using spectrophotometry to measure tablets and pure paracetamol was developed. The strategy is predicated on the drug interacting with the molybdate of ammonium in a very acidulous solution to create molybdenum blue. Beer's law was obeyed by paracetamol concentrations as high as 6 g/ml, and 0.10 g/ml was the detection limit (p = 0.05). At 670 nm, the molar absorptivity was 2.6 x 104 1/mol/cm, and the reaction's Sandell's sensitivity in this regard was 0.0059 gcm^2 each absorbance unit of 0.001 (Basilio Morelli, 1989).

A sophisticated technique was created for determining acetaminophen in medicines using direct FTIR spectroscopy. The process involves dissolving paracetamol in a 10% v/v ethanol solution in CH_2Cl_2 and measuring absorbance directly at 1515 cm^{-1}, with measurement correction using the 1900 cm^{-1} baseline that was set. A method can be carried out in the flow injection as well as the stopped-flow modes, with a sensitivity of roughly 0.09 A ml/mg in both cases and a threshold for detection of 8 g/ml in the mode of stopped-flow and 33 g/ml in the mode of flow injection (Zouhair Bouhsain *et al.,* 1996).

A device that gauges the transmission of whole tablets between 600 and 1900 nm in wavelength, spectra was captured. Using two multivariate calibration techniques, spectral data were analyzed, namely stepwise multiple linear regression (SMLR) and partial least squares regression (PLSR) (Eustaquio. *et al.,* 1999).

A straightforward and precise technique was created for determining the presence of acetaminophen in the formulations of pharmaceuticals. In the presence of 1ml HCl and 1ml acetic acid, 10.0 mg of sodium bismuthate was added after dissolving paracetamol in 4 ml sulfuric acid. It had a consistent color of bluish-violet. The colored chemical has a maximum of around 550 nm. The Beer's law was followed in concentration ranges from 100 to 300 g/m in 1ml HCl and 300 to 800 g/ml in 1M medium containing acetic acid and detection limits of 0.03 g/ml in 1ml HCl and 0.05 g/ml in 1m acetic acid medium, in that order (Pavan Kumar *et al.,* 2011).

Paracetamol spectrofluorometric determination in formulations of pharmaceuticals was developed. An easy and considerate way to determine paracetamol has been described, which is based on the paracetamol and cerium oxidation reaction. The species that glows is a cerium reduction item with stimulation as well as release wavelengths respectively, 255 and 348 nm. Fluorescence over the system, the intensity is linear. Paracetamol concentration has a detection range of 150-750 g/l with a relative standard deviation (RSD) of 1.22% and 20 g/l, respectively (Hossein and Hamid, 2011).

4.2 Chromatographic techniques

A high performance liquid chromatography in reverse phase method was created for identifying pharmaceutical formulations containing acetaminophen. The stationary phase of C18 is employed with a combination of methanol and water (1:2 v/v) flowing at 1.78 ml/min and at 193.3 nm of spectrophotometric detection. The internal standard sulphamethoxazole and the analysis take about 5 min (Sinan suzen *et al.,* 1998; Sujatha Samala *et al.,* 2022).

A high-performance liquid chromatography approach measuring pharmaceutical formulations of the quantity of acetaminophen was created. This only takes a few minutes and has sharp peaks that are noted. 20 cm x 4.6 mm of the column in stainless steel loaded with ocadesence and glued to permeable silica. It employs 10 mm and 0.2 ml per min through a 20-micrometre loop injector with a spectrum photometer set to 272 nm. The retention periods for 4-ammino phenol and sample solution are 4.388 and 4.542, respectively (Narwade, 2014; Jahnavi Bandla and Ashok Gorja, 2022).

A technique was created for determining the quantity of paracetamol in pharmaceutical preparations using the TLC densitometric approach. The drug is dissolved in methanol and then spotted onto a small amount of silica gel G254 using this procedure. On silica gel, paracetamol was separated using a mobile phase of ethyl acetate:benzene: acetic acid at an equation of 1:1:0.05 v/v/v. The absorption (or reflectance) of the divided medication was measured at a wavelength of 250 nm. Curves of calibration for paracetamol are created in the 5-20 mcg/spot concentration range. Quantification is possible by doing a comparison between the areas under the peaks discovered while scanning the thin-layer chromatographic plates in a spectral densitometer. An approach was utilized in formulations of pharmaceuticals, and the findings were compared statistically to the results acquired using the mode of reference (Nadia and Mostafa, 2010; Mohammed Zafar *et al.,* 2020).

A unique method for determining the kinetics was suggested for paracetamol in pharmaceuticals. The process is based on tracking concentration changes in a matrix reaction system using potentiometric monitoring that is close to the bifurcation point and in a stationary condition that is stable and not in equilibrium. In the matrix system, the bray-liebhafsky oscillatory reaction is employed situation under study. A Pt electrode measures the matrix system in response to disturbances generated by varied paracetamol focal points. The proposed method is based on a linear relationship between the

logarithms of the increased amounts of paracetamol and the maximum potential shift, Em. It is produced under optimal experimental conditions for paracetamol doses ranging from 0.0085 to 1.5 mol. The suggested method's sensitivity and precision were excellent, with a detection limit of 0.0027 µmol and 2.4% of R.S.D (Natasa Pejic *et al.,* 2006).

A distinct pulse voltammetry was used on a carbon ionic liquid electrode to develop a method for determining paracetamol. A conventional carbon paste electrode (TCPE) and a carbon ionic liquid electrode (CILE) were used to study the electrochemical behavior of paracetamol in 0.1 m acetate buffer solution (pH 4.6). The CILE was constructed by substituting conductive hydrophobic room temperature ionic liquid, 1-butyl-3-methylimidazolium hexafluoro-phosphate, for nonconductive organic binders. According to findings, the (CILE) displayed a greater ability to reverse based on the redox of paracetamol using electrochemistry. When the approach was employed to detect the presence of paracetamol, the average recovery was 99.3% in urine samples and 98.5 % in tablet samples (Shang Guan. *et al.,* 2008).

A method for determining the amount of API in paracetamol tablets using cyclic voltammetry was created and a glassy carbon electrode was used to detect the acetaminophen peak current in a pH 7.0 0.10 mol/l phosphate buffer. The best 0.0005 v was discovered to be the step potential and 0.1000 v/s to be the scan rate. Between 3 and 240 g/ml was the linear calibration range. With a 3.0 g/m as the detection threshold and recovery rate of 99.1% (Kanita Tungkananuruk *et al.,* 2005).

5. Conclusion

In conclusion, the development of analytical methods by HPLC for paracetamol/acetaminophen in the form of soft gelatin capsules. These tools can be used to assess this combination regularly in future advancements. This method is shown in this review for developing the analytical method of paracetamol in the HPLC technique. The detection and quantification limits of acetaminophen were determined to be 120 ng/ml and 360 ng/ml, respectively. The recovery and assay investigations of paracetamol were from 99 to 102%, it is clear that the proposed approach applies to the analysis of paracetamol quality control.

The development of innovative technologies for detecting and quantifying paracetamol in medicines, and environmental matrices is critical for avoiding and controlling its potentially harmful consequences. Given the possibility of paracetamol buildup efficient, delicate, and straightforward analytical techniques in surface water, drinking water, and wastewater is critical for detection. The HPLC analytical method has proven to be reliable for quality control of paracetamol/acetaminophen formulations with complicated compositions and may be used in standard analytical laboratories without the need for expensive instrumentation. As a result, the approach can be utilized for routine raw material analysis as well as *in vitro* dissolution studies of dose formulations including paracetamol.

Acknowledgments

The authors would like to express their gratitude to the management of Vels Institute of Science, Technology, and Advanced Studies (VISTAS), Pallavaram, Chennai, for providing all necessary facilities for the completion of this review study.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

Reference

Alloui, A.; Chassaing, C.; Schmidt, J.; Ardid, D.; Dubray, C. and Cloarec, A. (2002). Paracetamol exerts a spinal, tropisetron-reversible, antinociceptive effect in an inflammatory pain model in rats. Eur. J. Pharmacol., **443**:71-77.

Amino Shariae, A. and Khan, A. (2015). Acetaminophen: Old drug new issues. J. Endod., **41**:588-593.

Andersson, D. A.; Gentry, C.; Alenmyr, L.; Killander, D.; Lewis, S. E. and Andersson, A. (2011). TRPA1 mediates spinal antinociception induced by acetaminophen and the cannabinoid - tetrahydrocannabinol. Nat. Commun., **2**:79-87.

Andres Criado; Soledad Cardenas; Mercedes Gallego and Miguel Valacarcel (2000). Continuous flow spectrophotometric determination of paracetamol in pharmaceuticals following continuous microwave-assisted alkaline hydrolysis. Talenta., **53**(2):417-423.

Bannwarth, B.; Netter, P.; Lapicque, F.; Gillet, P.; Pere, P. and Boccard, E. (1992). Plasma and cerebrospinal fluid concentrations of paracetamol after a single intravenous dose of propacetamol. Br. J. Clin. Pharmacol., **34**:79-81.

Basilio Morelli (1989) Spectrophotometric determination of paracetamol in pure form and in tablet. J. Pharm and Bio. Anal., **7**(5):577-584.

Beauchamp, G.A.; Hart, K.W.; Lindsell, C.J.; Lyons, M.S.; Otten, E.J.; Smith, C.L.; Ward, M.J. and Wright, S.W. (2013). Performance of a multi-disciplinary emergency department observation protocol for acetaminophen overdose. J. Med. Toxicol., **9**(3):235-241.

Blyth, F.M.; Briggs, A.M.; Schneider, C.H.; Hoy, D.G.; March, L.M (2019). The global burden of musculoskeletal pain. Am. J . Public Health., **109**:35-40.

Dhritimoni Devi.; and Sumithra, M. (2023). Development and validation of analytical technique for the evaluation of insulin glargine by RP-HPLC. Ann. Phytomed., **12**(1):611-615.

Eustaquio, A.; Blanco, M.; Jee, R.D. and Moffat, A.C (1999). Determination of paracetamol in intact tablets by use of near-infrared transmittance spectroscopy. Analytica Chimica Acta., **383**(3):283-290.

Ghanem, C.I.; Perez, M.J.; Manautou, J.E. and Mottino, A.D. (2016). Acetaminophen from liver to brain: New insights into drug pharmacological action and toxicity. Pharmacol Res. Jul., **109**:119-31.

Gregorio Alapont, A.; Lahuerta Zamora, L. and Martinez Calatayud, J. (1999). Indirect determination of paracetamol in pharmaceutical formulations by inhibition of the system luminol–H_2O_2–$Fe_3(CN)_6$-chemiluminescence. J. Pharm. and Biomed. Analysis, **21**(2):311-317.

Hossein Tavallali and Yahya Hamid (2011). Spectrofluorometric determination of Paracetamol in pharmaceutical formulations. Asian J. pharm Res. Dev., **2**(1):11-17.

Jahnavi Bandla and Ashok Gorja (2022). Development and validation of sample simultaneous analysis for ertugliflozin and metformin by reverse phase-high performance liquid chromatography (RP-HPLC) in tablet dosage form. Ann. Phytomed., **11**(1):83-90.

Kanita Tungkananuruk; Nipon Tungkananuruk and Duncan Thorburn Burns (2005). Cyclic voltammetric determination of acetaminophen in paracetamol tablets. KMITL Sci. Tech. J., **5**(3):160-164.

Krishna, K.; Verma and Archana Jain (1985). Spectrophoto-metric determination of paracetamol with iodobenzene. Talanta., **32**(3):238-240.

Lee, S.K. Quinonez, R.B. Chuang, A. Munz, S.M. Dabiri, D. (2016). The case for improved interprofessional care: Fatal analgesic overdose secondary to acute dental pain during pregnancy. Case Rep. Dent., **16**:746-762.

Martinez Calatayud, J.; Pascual Marti, M.C. and Sagrado Vives, S. (1986). Determination of paracetamol by a flow injection-spectrophoto-metric method. Analytical Letters, **19**:19-20.

Mohammed Zafar; Mohammed Abdul Rasheed Naikodi; Kommu Nagaiah and Sunder Raju, P.V. (2020). Development of standard operating procedures and quality standards of kushta gaodanti with HPTLC fingerprinting and hyphenated techniques. Ann. Phytomed., **9**(1): 66-77.

Narwade, S. S. (2014). Qualitative and quantitative analysis of paracetamol in different drug samples by HPLC technique. J. Appl Chem., **7**(8):46-49.

Nadia, M. and Mostafa (2010). Stability indicating method for the determination of paracetamol in its pharmaceutical preparations by TLC densitometric method. J. Saudi Chem. Soc., **14**(4):341-344.

Natasa Pejic.; Ljiljana Kolar-Anic and Slobodan Anic (2006). Determination of paracetamol in pure and pharmaceutical dosage forms by pulse perturbation technique. J. Pharm. Biomed. Anal., **41**(2):610-615.

Pavan Kumar, G.V.S.R.; Bhuvan Kumar, G; Chandra Sekhar, T.; Sreerama and Murthy, B.(2011). Spectrophotometric determination of paracetamol using sodium bismuthate as chromogen, IJRCE., **2**(1):231-235.

Raghavi. R.; Vijey Aanandhi, M. and Sumithra, M. (2023). Analysis of phytoconstituents and its phytoformulation of curcumin chewable tablet as per ICH guidelines, Ann. Phytomed., **12**(1):601-605.

Salah Sultan, M. (1987). Spectrophotometric determination of paracetamol in drug formulation by oxidation with potassium dichromate. Talanta., **34**(7):605-608.

Shang Guan, X.; Zhang, H. and Zheng, J. (2008). Electrochemical behavior and differential pulse voltammetric determination of paracetamol at a carbon ionic liquid electrode. Anal. Bioanal. Chem., **391**(3):1049-55.

Sinan Suzen.; Cemal Akay.; Aenol Tartilmis.; R. Serdar Erdol.; Atilla Onal and Aemsettincevheroglu. (1998). Quantitative of acetaminophen in pharmaceutical formulation using HPLC. Fac. J, Pharm., **27**(2): 93-100.

Sridhar Narayan; Pradeep Kumar; Rakesh K Sindhu; Ayushman Tiwari and Manik Ghosh (2009). Simultaneous analysis of paracetamol and tramadol - analytical method development and validation. Der. Pharma. Chemica., **1**(2):72-78.

Sujatha Samala; Palatheeya Sujatha and Tharun. G. (2022). Method development and validation of bendamustine HCl injection by using RP-HPLC. Ann. Phytomed., **1**:95-100.

Subhamalar, K.; Vijey Aanandhi, M. and Afroz Patan (2023). Analytical method development and validation of rifaximin and ornidazole in bulk and combined tablet dosage form as per ICH guidelines. Ann. Phytomed., **12**(1):595-600.

Vimal Raj, M. and Sumithra, M. (2023). Analysis of second-generation antihistamine fexofenadine soft gelatin capsules and its related compound by using RP-HPLC. Ann. Phytomedicine., **12**(1):616-627.

Zouhair Bouhsain; Salvador Garrigues and Miguel de la Guardia (1996). Flow injection-Fourier transform infrared spectrometric determination of paracetamol in pharmaceuticals. Analyst., **121**:635-639.

Citation **R. Gandhimathi, V. Nivathra, and C. M. R. Kajhareshevarmaa (2023). An overview of analytical methods for quantification of paracetamol. Ann. Phytomed., 12(2):299-303. http://dx.doi.org/10.54085/ap.2023.12.2.37.**