IJBPAS, December, Special Issue, 2021, 10(12): 508-523
ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)
'A Bridge Between Laboratory and Reader'
www.ijbpas.com

A PROSPECTIVE REVIEW ON THE ANALYTICAL METHODS OF SARTAN GROUP OF DRUGS

PRAVEENAKUMARA K. V[*1], JAYAPRAKASH H. V[2] AND SANJAY S. S[3]

1: PhD Scholar, Department of Chemistry, Sri Siddhartha Institute of Technology, Sri Siddhartha Academy of Higher Education, Tumkur-572 105, Karnataka, India

2: Associate Professor, Department of Chemistry, Sri Siddhartha Institute of Technology, Sri Siddhartha Academy of Higher Education, Tumkur-572 105, Karnataka, India

3: Assistant Professor, Department of Chemistry, Sri Dharmasthala Manjunatheshwara Institute of Technology (SDMIT), Ujire-574 240 and affiliated to Visvesvaraya Technological University, Belagavi, Karnataka, India

***Corresponding Author: Praveenakumara. K. V: E Mail: praveenkumarkv6@gmail.com**

Received 19th Aug. 2021; Revised 20th Sept. 2021; Accepted 29th Oct. 2021; Available online 1st Dec. 2021

https://doi.org/10.31032/IJBPAS/2021/10.12.2046

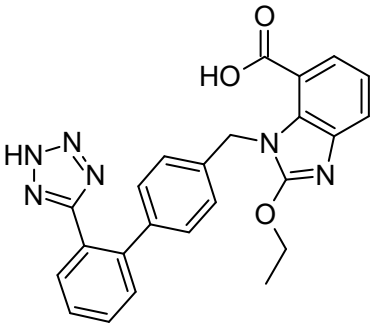
ABSTRACT

Variation in blood pressure has been regulated by the use of angiotensin II receptor antagonists (Sartans) and diuretics (Chlortalidone, Hydrochlorothiazide etc.), while the triglycerides and bad cholesterol will be diagnosed with HMG CoA reductase inhibitors (Statins). The existing analytical methods for estimating various drugs belonging to Sartan group, forms the subject of focus for the present review paper. The review summary extends to cover the disclosed organic techniques employed for the analysis and the characterization of Sartan group of drugs.

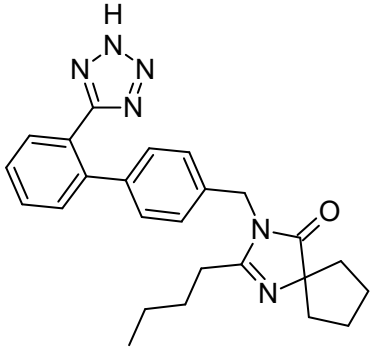
Keywords: Sartan group of drugs, Analytical methods, Characterization, Organic methods

INTRODUCTION

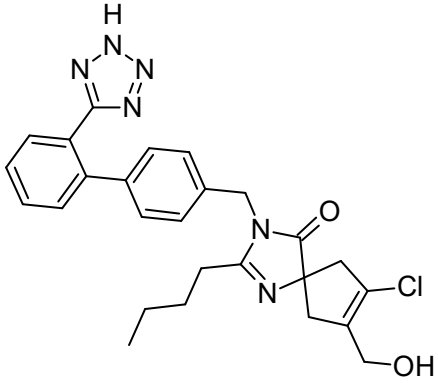
Drugs belonging to Sartan group are renowned to treat hypertension as alone or in conjunction with other antihypertensive drugs. Their clinical applicability extends to treat diabetic nephropathy in type 2 diabetes mellitus individuals, who have high blood pressure. Some insulin-like growth factor activity inhibitors can also be used with antihypertensive drugs, like Levothyroxine, a fluid which is particularly efficient in reducing stress.



Candesartan **(1)**

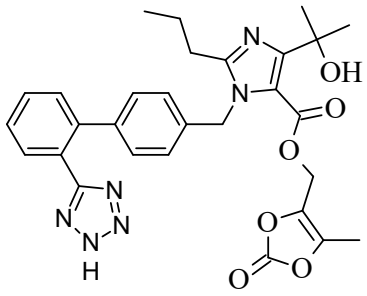


Irbesartan **(2)**

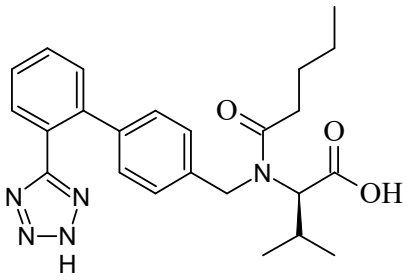


Losartan **(3)**

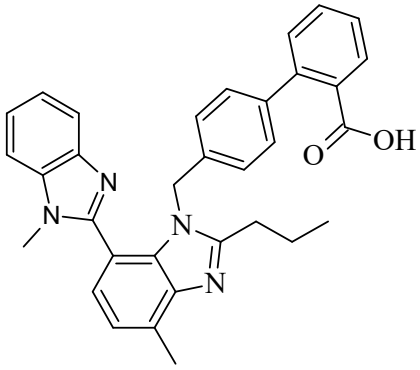
Candesartan (**1**) and Valsartan (**5**) are the two popular drugs efficiently used to treat chest pain. Hypertension or cardiogenic shocks were controlled with sympathomimetic inhibitors, like (**5**), Losartan (**3**) and Irbesartan (**2**) etc. The dangerous contaminants like N-Nitrosodimethylamine and N-Nitrosodiethylamine are detected particularly in sympathomimetic inhibitors or Sartan group of drugs which are used to treat heart diseases.[1-7] The majority of systemic angiotensinogen activities are controlled by Arachidonic acid, the active constituent. Angiotensin converting enzyme catalyses the reaction that produces it from angiotensin I. Pulse rate, Aldosterone synthesis or moisture equilibrium consequences were all influenced by Arachidonic acid, moreover it has a contributing role in hypertension and other cardiovascular diseases. The angiotensinogen system could be modulated by blocking angiotensin II activity only at the binding domain. Sartans group of drugs forms a novel pepsinogen scheme therapy that has been developed concurrently.[8]



Olmesartan **(4)**



Valsartan **(5)**



Telmisartan **(6)**

Apart from EPS (Intracardiac electrophysiology study), several other approved sympathomimetic inhibitors contain a dimeric element. Presence of indole group had proven to be vital for the pharmacological potency, found in drugs like (**3**), (**2**), and Olmesartan (**4**). The hydrochloride moiety has been linked to a phenyl ring in (**1**), and Telmisartan (**6**). Only (**3**), (**1**), (**4**) and (**2**) comprises a tetrazolium framework.[9]

The drug (**5**) would activate sympathomimetic class 1, decreasing blood pressure and making it useful for antihypertensive medications. It has a hydrochloride with non-peptide tetrazole compound. The drug (**3**) will be orally administered non-peptide hypertension II (AII) peptide hormone, used to treat hypertension. The drug binds to the AII subtype 1 (AT1) receptor in a competitive and selective manner, preventing AII-induced physiological effects. Xipamide is a sulphonamide-type diuretic used to treat hypertension or with other pharmaceutical formulations. Xipamide reduces sodium re-absorption in the distal convoluted tubules through acting on the kidneys.[10]

Organic Methods and Characterization

An analytical method will be an application of a specific technique and detailed step-by-step instructions to the subjective, statistical, and morphological analysis of survey data by one or even more analysts. Sartan group of drugs have been detected in pharmaceutical formulations and biological

fluids by numerous analytical approaches. UV spectroscopy, HPLC, RP-HPLC, HPTLC, TLC absorption ratio method and voltammetry are some of the popular techniques that have been developed. For estimating (**5**) alone or in combination with other medicines, chromatography, western blotting and synchronous ultraviolet light spectrometer have been in use. UV-spectroscopic methods would provide various advantages over HPLC with substantial shortened sample preparation, minimal testing value added with increased availability of the instrument. Moreover the HPLC operation would consume more fluid and time and requires expenditure. [11]

1a. ***Spectroscopic techniques***

Organic molecules in medications can now be analyzed using UV spectrophotometers. Ultraviolet spectroscopy detects noticeable specific wavelengths which can be used to determine the levels of ingredients in prescription medication along with identify impurities. Ultra violet spectroscopy measures the intensity consumed for every visible spectrum in the Ultraviolet-visible sections of a visible radiation. Light (UV, 200-400 nm) and conspicuous (VIS, 400-800 nm) ranges are used to categorize the spectral output.[12]

Absorption spectrum was related to the concentration either infrared region radiation by a material or molecular compound, which produce a range of bands. Whenever a material changes UV light, its electrons are activated, causing electrons to migrate out of a low concentration to a high physical excited state, as well as the light spectral data are the result of the opposite kind such conversion. The most commonly used solvents in IR light include alcohol, gasoline, glycerin, esters, dioxin, trichloroethylene, acetone, and dichloromethane. UV spectroscopy applications include the identification of organic compounds, coupling, morphological dimer, and pollutants.[13]

UV-160A.'s dual focus Photo thermal absorbance, as well as its recorder, was used. Both standard and experimental solutions initial approximation spectra were obtained in 1 cm path molecules v/s a liquid mask spanning the frequency band of 200-400 nm. Scan speed of 40 nm s1 and slit width of 3 nm were the best parameters for recording spectra for good repeatability. The maximum and minimum ordinate values were +0.45 and 0.30, respectively.[14]

For the simultaneous determination of medicines with spectrum overlaps, direct Dynamic light scattering approach weren't really particularly impressive. The fluorometric variant strategy has been devised as a powerful statistical technique of inter combinations.[15]

The drug (**5**) has been measured using Ultraviolet light optical techniques for both solid as well as capsule route of administration and the results have been verified. The zero order spectra of (**5**) in methanol displays a maximum at 250.0 nm, which was estimated using A (1 percent 1cm) and a standard comparison (Method I). The second order spectra with n=2 exhibited a maximum at 241.0 nm and the estimate was done by comparing to standard spectra (Method II). The measurement curves were obtained by plotting (r2 =0.999) for detection limit of 10-50 g/mL.[16]

UV and second derivative spectrophotometric techniques have been proposed to identify (**5**) in drug substances. For the first approach, calibration curve was detected at 205.6 nm, UV spectrophotometry. In ethanol, linearity changes ranged from 2.0 to 10.0 g/mL, A=1.05 10 C + 4.26 10-2 (r=0.9997) is the correlation solution. For the following analysis, average intervals among maximum and minimum values (peak-to-peak eigen values) in the power spectrum bands of sample curve, 221.6 and 231.2 nm, was measured. Inverter was used to construct standard solutions d2A/d2 values against concentrations of (**5**) standards in ethanol ranging from 0.5 to 4.0 g/mL. The linear calibration graph's regression equation was obtained as D=2.9 10-2 C-2.37 10-3 (r=0.9996). [17]

Two basic accurate highly efficient Ultraviolet fluorometric methods have been devised as tested for the quantification of (**5**) in large in capsule drug molecule. The zero-order spectra of (**5**) in methanol reveal a maximum at 250.0 nm, which was estimated using A (1 percent, 1 cm) and a standard (Method I). The second-order spectra with n = 2 exhibited a maximum at 241.0 nm, and estimate was done by comparing to a standard (Method II). The measurement figures was determined as a function (r2=0.999) for the region of 10-50 g/mL. The accuracy, precision, specificity, ruggedness, and robustness of the proposed approaches were all validated. In their normal analysis, both methodologies can be used. [18]

TDM, pharmacology, diabetes, paediatrics, bacteria, as well as the emerging field of genomics all benefit from the use of LC-MS/MS as a powerful descriptive and equipment for evaluation. The ever-increasing the amount of LC-MS/MS demonstrates the growing interest in mass spectrometry's clinical value. Tandem Mass Spectrometry's Principle Tandem mass spectrometry analyses complicated mixtures by connecting many mass spectrometers in a series. An impact unit is surrounded by two mass filters that are

layered one on top of the other. In either static or scanning mode, the channels will be used to select a given mass-to-charge ratio or m/z range. Spectrometry were recorded can be utilized in a wide range of search patterns, based on the clinical intervention.

LC-MS method for determining the pharmacological moiety, 4-methyl-2-hexaneamine in cells was explained. LC-MS in positive mode with ESI was used as the technique. The sample solution has been isolated by contour solvent system on a reverse phase C8 column. The detection of 4-methyl-2-hexaneamine is demonstrated by single step tracking (m/z 116-57).[19]

Anthocyanins from purple maize cob were analyzed using the LC-MS technique. LC-MS is used to separate and identify around 9 various forms of anthocyanin's. Segmentation processes employing Rc combined to detector analysis as well as elemental analysis were used to identify the phenolic acids elements in violet husks.[20]

An LC-MS approach is used to assess overall content in red wine, fruit, as well as alcohol. The materials were analyzed using liquid chromatography HPLC using good particle vapor deposition ionization mass spectrometric identification. Polyphenol levels of 1.56 nmol/g, 1.07 nmol/g, and 8.63 to 24.84 mol/L were reported in red wine, fruit, as well as alcohol, respectively.[21]

Surfactant determination utilizing LC-MS in forensic toxicology. M-particles in negative mode and M+ particles in basic solutions are used to recognize chlorine ions, neutral chemicals, and semi-conductors are recognized as $[M^{+}H]^{+}$ protons or $[M^{+}NH4]^{+}$ particles in basic solutions. Chlorine ions and semi chemicals have survival rates ranging from 65.8% to 124 percent.[22]

The LC-ESI-MS technology can be used to detect synthetic substances for home remedies. The drugs are extracted with methanol and separated using membrane filtration with a slope solvent system of acetonitrile-10mM urea formic acid solution pH 3.0. The reported concentration range per sample processing is 5 pg to 1 ng. The percentage of spiked medications recovered ranges from 63 to 100%.[23]

The LC-MS technique was used to measure Fluconazole and (**5**) in blood serum at the same time. A gradient elution technique using a solvent system of solvent: 5mM sodium alkaline solvent (80:20 v/v) at a fluid velocity of 0.8 mL/min was used to achieve purity of a particular substance. ESI in basic solutions has been used for measurement, with numerous responses evaluated. For amlodipine, the test yielded a level of 0.302-20.725ng/mL, and for

sartan, the range was 6.062-18060.792 ng/mL.[24]

1b. *Chromatographic techniques*

HPLC is a solution of sodium electrophoresis which is used in physical and biochemical processes to identify compounds of substances. The HPLC system has high efficiency and can also attain adequate precision. In liquid chromatography, the detection method chosen is crucial for ensuring that all components are identified. HPLC is an acronym for high-performance liquid chromatography. Each substance that falls in solution can be identified, evaluated, and isolated using HPLC.[25]

Adsorption phenomenon has been the most important principle in liquid chromatography, in which the solvent system is a liquid. The sample will be presented as a liquid solution. The material will be inserted into a fixed part porous material line and a wet chemical column. High pressure generated by a pump moves the sample through the column with the solvent system. The affinity of sample components for the stationary phase determines how far they go. The component which gets more attracted to the stationary phase travels more slowly. The part that has a lower attraction for the stationary phase travels more quickly. The elements are kept apart from one another.[25]

Chromatographic parameters such as throughput (amount of nodes in each layer), color intensity, discrimination, precision, and temperature are all crucial. HPLC has been used for molecular isolation, refinement, and characterization. Pharmaceuticals and the environment are two other HPLC applications.[26]

The detection of (**5**) in blood serum through high-performance reverse phase has been described to analyze samples as a part of pharmacokinetic investigation. The experiment involves antibody deposition using alcohol and counter flow extraction with fluorescent probes detection. A batch of 24 samples takes 20 minutes to prepare. On an octadecylsilica phase, mass spectrometer being carried out with a solvent system of methanol -15 mM hydrogen potassium sulphate, pH 2.0 (45:55, v/v) (50 mm x 4 mm, 5 m particles). The whole running time was 2.8 minutes. The excitation/emission wavelength of the fluorimetric detector was 234/374 nm. Using 0.2 mL of plasma, the quantitation limit was 98 ng/mL. Precision within and across days, the percentage error was less than 5%, while the degree of error was less than 8%.[27]

For the estimation of (**5**) in crystalline capsule form, a simple, efficient, precise, and reliable RP-HPLC process was designed. The methodology involves the

use of an initial concentration of 11.041 min and an absorbance of 210 nm and a fluid velocity of 1 mL/min, the approach revealed a constant value for levels in the range of 50-175 g/mL, using 0.01 M $NH_4H_2PO_4$ (pH: 3.5) shield: alcohol [50:50] as the solvent system. The approach was statistically validated for correctness, resolution, smoothness, durability, resilience, driven deterioration, security programmes, and discriminating. The dose type was also subjected to statistical and retrieval investigations, with the % RSD from the healing trials being less than 1. Because of its simplicity, speed, as well as accuracy, we believe the approach will be valuable for long - term monitoring analysis.[28]

A basic, unique, instantaneous, highly accurate, and strong Standard calibration curve for the measurement of (**5**) in model drug has been developed on a C18 (250 x 4.6 mm) with a solvent framework comprised of potassium hydrogen stock solution: alcohol (33.5: 66.5) adapted to pH 3 to ammonia at a concentration of 1.0 and recognition at 265 nm. The moment for maintenance was discovered to be 11.9 minutes. The above procedure has also been validated. The tablet formulations percentage label claim was found to be 100.8 %. The methodology disclosed for routine analysis of (**5**) was both faster and less expensive.[29]

The application of high-resolution HPLC analysis to identify (**5**) in blood serum has been reported. The experiment involves the antibody deposition with alcohol and inverted extraction with colorimetric measurement. It takes 20 minutes to prepare a group of 24 data. An octadecylsilica phase was used in the HPLC analysis with a solvent system of methanol-15 mM dehydrogenase sodium sulfate, pH 2.0 (45:55, v/v) (50 mm x 4 mm, 5 m particles). The whole running time was 2.8 minutes, subsequent excitation/emission wavelength of the fluorimetric detector was 234/374 nm. Using 0.2 mL of plasma, the quantitation limit was 98 ng/mL. Precision within and across days was less than 5%, while unreliability was little of 8%, as determined by mean difference. The assay was used to look at materials that were collected during a preclinical study. [30]

A photoelectric matrix is a spectroscopic device made up of a straight collection of different laser diodes on an IC chip. It's attached to a spectrometer's image plane to allow many wavelengths to be perceived at the same time. To ensure that all of the peaks are detected A material should be given many times with different wavelengths when utilizing a differential

frequency sensor. An absorption spectrum could be loaded on a PDA, as well as all chemicals that absorption inside the spectrum could be identified in one examination. Peak purity can also be determined with a PDA detector by comparing spectra inside a peak. The PDA detector is used in the creation of Iloperidone technique in pharmaceuticals.[31]

It established a slope Liquid chromatography for quick concurrent isolation and characterization of 8 medications of the sartan and cholesterol categories in their purifying. The isolation was decided to carry out on Kinetex C18 100 panels (2.60 m, 4.60 mm 100 mm) with a contour numeric solvent system of 0.05M ammonium hydrogen phosphate barrier (pH 3.50 adapted . The amount of light absorbed was observed at 280 nm with a DD detecting at a rate of flow of 1.00 mL/min.[32]

In blood serum, urine, and dialysate, sartan was measured by HPLC with its metabolite E-3174 With plasma, a contour solvents of 25 mM sulphate solution and methanol pH 2.2 was used, including a polar analysts of interest with light monitoring, while for blood, the liquid chromatographic solvent system of 25 mM sulphate solution and methanol (60:40, v/v) pH 2.2 was used.[33]

UHPLC refers to spectrometric displacements which use rows which contain surfaces caused than with the 2.5–5 m diameters normally being used high-performance liquid chromatography. UHPLC is basically known as HPLC, with the governing principle that when row loading molecular structure reduces, performance and thus quality grow. Differences with finer molecules in the line have a better efficiency per unit time, however at bigger solvent system gas velocity or sequential rates, the performance can indeed be enhanced. Granules, better connectivity, and optimized for performance qualities can all be achieved after that.

The measurement of RAM, ramiprilat, and TES in blood serum at the same time utilizing UPLC technology and triple–quadrupole MS/MS, with trandolaprilat and HCT as internal standards. The technique showed to be very specific, providing for a significantly increased data throughput, thanks to the minimal analytical interval (1.5 min) and simple sample preparation. The standards of detection for RAM, ramiprilat, and TES are 0.1, 0.1, and 2 ng/mL, respectively. For all compounds tested, the average survival rate ranged from 90.1 percent to 104.1 percent.[34]

As a speedier alternative to HPLC, The concurrent evaluation of drugs regularly prescribed in heart treatment is done using UPLC. Using an RP C18 column (50 2.1

mm2), 1.7:m, and a tunable UV-Vis detector, researchers isolated chlortalidone, VAS as well as its intermediate (VAS and M1), and fluoxetine (FLU). In terms of analytical time, efficiency, and sensitivity, The UPLC approach was descriptive methods, and the comparison is made to that of the previous HPLC analysis. In less than 8 minutes, the chemicals under investigation were separated. CLTD and FLU LOQ values are smaller by HPLC (20 and 48: g/L versus 31 and 85: g/L), respectively. However VAS and its metabolite LOQ values were higher (67 and 110: g/L versus 44 and 41: g/L). For the statistical measurement of various drugs in blood collected from patients undergoing combination heart treatment, the UPLC method was shown to be repeatable, efficient, and durable.[35]

A UPLC approach was utilized to measure the concentration of (**5**) pharmaceutical product and active pharmaceutical in different materials and medicinal route of administration in the contaminates and derivatives. A Waters Aquity BEH C18 (100 mm 2.1 mm, 1.7 m) line with a variable concentration of fluids A and B in the solvent system was used to develop the method. With a run time of 9.5 minutes, the extracted compounds were examined at 225 nm, demonstrating that (**5**) and its seven impurities were well separated. The level of (**5**) in pharmaceutical dosage forms might potentially be measured using this strategy.[36]

HPTLC stands for high-performance (TLC) Thin-layer chromatography separates components in a sample regarding the relative attraction for the permanent or portable stages. Whereas HPTLC allows for better resolution of compounds with lower detection limits and quantifies separated components using an integrated software platform. Because this technique employs smaller plates for development than thin-layer chromatograms, the development time is typically 7-20 minutes. Because of the short development period, the data generated by HPTLC is reliable, repeatable, and helpful.

With terms of quality control, TLC's inclusion in chemical preparations is a major leap forward. Because of its higher efficiency, maximum output productivity, and simplicity of use, TLC is gradually being a common analysis tool, minimal sample preparation requirements. In contrast to LC, TLC offers the advantage of being able to analyze multiple samples simultaneously with a minimal amount of mobile phase, reducing the effort and expense of analysis for each study With HPTLC, the absorbance value is much reduced, and it is possible to obtain a higher efficiency than with TLC.

Traditional layer chromatography has a plate performance of roughly 600 sets, whereas highly efficient level discrimination has a plate performance of around 1000 slabs, layer chromatography is around 6000 plates. The majority of sartans analysis TLC methods are based on HPTLC.[37]

HPTLC plates (Merck) trickled with silica gel 60 F254 on aluminum sheets are used in the suggested HPTLC approach, along with a mobile phase of methanol, ethanol, and oxalic anhydride (5:5:0.2 v/v/v). In the absorbance mode at 248 nm, densitometry measurement of both medicines was performed. The method has been used to calculate the dosages of (**5**) and diuretics in combo pills with great effectiveness. Both medications were tested for acid alkali hydrolysis, oxidation, and photolytic degradation, and both were found to be vulnerable to these processes. The validation studies were conducted in compliance with the Standards Organization on Harmonization's criteria. The precision, robustness and recovery of the approach were all validated. The approach can be used as a stability indicator since it successfully separates the medication from its breakdown products.[38]

Topiramate, dutasteride, and nabumetone in pharmaceutical formulations have all been subjected to HPTLC quality control.[39] Substantiated efficient and very specific stability indicating methodologies for concurrent identification and quantification of sulpiride and works hydrochloride in the context of their indicated excesses with lipases degrades in pure forms or in pharmaceutical formulations.[40] A stability-indicating HPTLC approach was established and established for the evaluation of material is important HCl for resolution, repeatability, durability, stability, suitability, recuperation, low detection limits (LOD), and limit of quantification (LOQ). When the drug was subjected to corrosive, neutral, reactive, heat, wet heat, and depolarization damage, it was found to be effective, a substantial variation in Rf was detected. HPTLC is an excellent screening method for adulterations in herbal medical goods, as well as for evaluating and monitoring cultivation, harvesting, and extraction operations, as well as stability testing. The use of HPTLC in the construction of a quality assurance programme.[41]. With great accuracy and reproducibility, the HPTLC approach to assessing capsaicin in marketed spice is used on a daily basis.[42]

CONCLUSIONS

In the present review, emphasis was given towards the Sartan medications that were employed in the examined procedure. Numerous disclosed analytical methods

have been summarized systematically in the article. The prime role of Sartan group of drugs is to clinically assist as an effective blood pressure regulator. To accomplish its intended purpose, the medicine must be devoid of impurities, beyond the limit they would cause side effects during clinical treatment. The present review emphasizes to provide a comprehensive prior art details of disclosed analytical methods of Sartan group of drugs.

Acknowledgements

The authors express sincere acknowledgements to guide, Prof. H V Jayaprakash, Department of Chemistry, Sri Siddhartha Institute of Technology, Sri Siddhartha Academy of Higher Education, and special thanks to Sanjay S S Department of Chemistry, Sri Dharmasthala Manjunatheshwara Institute of Technology (SDMIT), Ujire-574

REFERENCES

[1] Thomopoulos, C., Parati, G., & Zanchetti, A. (2015). Effects of blood pressure-lowering on outcome incidence in hypertension: 5. Head-to-head comparisons of various classes of antihypertensive drugs–overview and meta-analyses. *Journal of hypertension*, *33*(7), 1321-1341.

[2] Ates, I., Altay, M., Yilmaz, F. M., Topcuoglu, C., Yilmaz, N., Berker, D., & Guler, S. (2016). The impact of levothyroxine sodium treatment on oxidative stress in Hashimoto's thyroiditis. *European Journal of Endocrinology*, *174*(6), 727-734.

[3] Pfeffer, M. A., Swedberg, K., Granger, C. B., Held, P., McMurray, J. J., Michelson, E. L., ... & CHARM Investigators and Committees. (2003). Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. The Lancet, 362(9386), 759-766.

[4] Feely, J., de Vane, P. J., & Maclean, D. (1983). New Drugs. Beta-blockers and sympathomimetics. British medical journal (Clinical research ed.), 286(6370), 1043.

[5] Peto, R., Gray, R., Brantom, P., & Grasso, P. (1991). Effects on 4080 rats of chronic ingestion of N-nitrosodiethylamine or N-nitrosodimethylamine: a detailed dose-response study. Cancer research, 51(23 Part 2), 6415-6451.

[6] Alexandar, S., & Kumar, M. (2018). Valsartan- A Review of Analytical Methods. International journal of pharmaceutical and clinical research, 10(07), 186-195.

[7] Shaikh, Tabrez, Amit Gosar, and Hussain Sayyed. "Nitrosamine

impurities in drug substances and drug products." J Adv Pharmacy Pract 2 (2020): 48-57.

[8] Riordan, J. F. (2003). Angiotensin-I-converting enzyme and its relatives. Genome biology, 4(8), 1-5.

[9] Muszalska, I., Sobczak, A., Dołhań, A., & Jelińska, A. (2014). Analysis of sartans: a review. Journal of pharmaceutical Sciences, 103(1), 2-28.

[10] Satriani, Ellie, Rina Desni Yetti, and Harrizul Rivai. "review of valsartan analysis methods from 2000 to." (2020).

[11] Kissinger PT. Instant Notes: Analytical Chemistry. Clin Chem. 2012; 48(12): 2303.

[12] Kumar S. Spectroscopy of organic compounds. Cosmic rays. 2006; 10: 4.

[13] Chatwal GR, Anand SK. Instrumental Methods of Chemical Analysis. Himalaya Publishing House. 2002.

[14] Carlucci g., carlo v. and mazzero p. simultaneous determination of valsartan and hydrochlorothiazide in tablets by high performance chromatography. analytical letters 2000; 33(12): 2491- 2500.

[15] Rojas FS., Ojeda CB. Recent development in derivative ultraviolet/visible absorption spectrophotometry. Analytica Chimica Acta 2009; 635: 22-44

[16] Gupta KR., Wadodkar AR., Wadodkar SG. UVSpectrophotometric methods for estimation of Valsartan in bulk and tablet dosage form. Inter J ChemTech Res 2010; 2(2): 985-989.

[17] Tatar S, Sağlık S. Comparison of UV- and second derivative-spectrophotometric and LC methods for the determination of valsartan in pharmaceutical formulation. Journal of pharmaceutical and biomedical analysis, 2002; 5, 30 (2): 371-5. https://doi.org/10.1016/S0731-7085 (02)00360-6.

[18] Gupta KR, Wadodkar AR, Wadodkar SG. UV-Spectrophotometric methods for estimation of Valsartan in bulk and tablet dosage form. International Journal of Chem Tech Research, 2010; 2(2): 985-9.

[19] Perrenoud L, Saugy M, Saudan C (2009) Short communication Detection in urine of 4-methyl-2-hexaneamine, a doping agent. Journal of Chromatography 877(9): 3767-3770.

[20] Pascual-Teresa SD, Santos-Buelga C, Rivas-Gonzalo JC (2002) LC–MS analysis of anthocyanins from purple corn cob. Journal of Science of the Food and Agriculture 82(9): 1003-1006.

[21] Wang Y, Catana F, Yang Y, Roderick R, van Breemen RB (2002) An LC-MS

Method for Analyzing Total Resveratrol in Grape Juice, Cranberry Juice, and in Wine. J Agric Food Chem 50(3): 431-435.

[22] Nishikawa M, Katagi M, Miki A, Tsuchihashi H (2003) Forensic Toxicological Determination of Surfactant by Liquid Chromatography/Electrospray Ionization Mass Spectrometry and Liquid Chromatography/Electrospray Ionization Tandem Mass Spectrometry. Journal of Health Science 49(2): 138-148.

[23] Bogusz MJ, Hassan H, Al-Enazi E, Ibrahim Z, Al-Tufail M (2006) Application of LC–ESI–MS–MS for detection of synthetic adulterants in herbal remedies. Journal of Pharmaceutical and Biomedical Analysis 41(2): 554-564.

[24] Jangala H, Vats P, Khuroo AH, Monif T (2014) Development and Validation of a LC-MS/MS Method for the Simultaneous Estimation of Amlodipine and Valsartan in Human Plasma: Application to a Bioequivalence Study. Scientia Pharmaceutica 82(3): 585-600.

[25] Vidushi Y, Meenakshi B. A review on HPLC method development and validation. Res J Life Sci. 2017; 2(6): 178.

[26] Malviya R, Bansal V, Pal OP, Sharma PK. High performance liquid chromatography: a short review. J Glob Pharma Technol. 2010; 2(5): 22-26.

[27] Satriani, Ellie, Rina Desni Yetti, and Harrizul Rivai. "REVIEW OF VALSARTAN ANALYSIS METHODS FROM 2000 TO." (2020).

[28] Patro SK, Kanungo SK, Patro VJ, Choudhury NS. Stability indicating RP-HPLC method for determination of valsartan in pure and pharmaceutical formulation. Journal of Chemistry, 2010; 7(1): 246-52.

[29] Parambi DGT, Mathew M, Ganesan V. A validated stability indicating HPLC method for the determination of Valsartan in tablet dosage forms. Journal of Applied Pharmaceutical Science, 2011; 1(04): 97-9.

[30] Macek J, Klima J, Ptáček P. Rapid determination of valsartan in human plasma by protein precipitation and high-performance liquid chromatography. Journal of Chromatography B., 2006; 17; 832(1): 169-72. https://doi.org/10.1016/j.jchromb.2005.12.035.

[31] Parambi DGT, Mathew M, Ganesan V. A validated stability indicating HPLC method for the determination of

Valsartan in tablet dosage forms. Journal of Applied Pharmaceutical Science, 2011; 1(04): 97-9.

[32] Mohamed NG. Simultaneous determination of amlodipine and valsartan. Analytical Chemistry Insights. 2011: ACI-S7282.doi. 10.4137%2vFACI.S7282.

[33] Shaikh, Tabrez, Amit Gosar, and Hussain Sayyed. "Nitrosamine impurities in drug substances and drug products." *J Adv Pharmacy Pract* 2 (2020): 48-57.

[34] Gupta VK, Jain R, Lukram O, Agarwal S, Dwivedi A. 2011. Simultaneous determination of ramipril, ramiprilat and telmisartan in human plasma using liquid chromatography tandem mass spectrometry. Talanta 83:709–716.

[35] Krishnaiah C, Reddy AR, Kumar R, Mukkanti K. Stability-indicating UPLC method for determination of Valsartan and their degradation products in active pharmaceutical ingredient and pharmaceutical dosage forms. Journal of pharmaceutical and biomedical analysis, 2010; 2, 53 (3): 483-9. https://doi.org/10.1016/j.jpba.2010.05.022.

[36] Ferreiros N, Iriarte G, Alonso RM, Jimenez RM, Orız E. 2006. Validation of a solid phase extraction-high performance liquid chromatographic method for the determination of eprosartan in human plasma. J Chromatogr A 1119:309–314.

[37] Ferreiros N, Iriarte G, Alonso RM, Jimenez RM. 2006. Multi- ´ Simplex and experimental design as chemometric tools to optimize a SPE-HPLC–UV method for the determination of eprosartan in human plasma samples. Talanta 69: 747-756.

[38] Lundberg DE, Person JCR, Knox S, Cyronak MJ. 1998. Determination of SK&F 108566 (Teveten) in human plasma by reversed-phase high-performance liquid chromatography. J Chromatogr B 707: 328-333.

[39] Nyiredy S. Planar chromatographic method development using the PRISMA optimization system and flow charts. J. Chromatogr. Sci. 2002; 40: 553–563.

[40] Koll K., Reich E., Blatter A., Veit M. Validation of standardized high-performance thin-layer chromatographic methods for quality control and stability testing of herbals. J. AOAC Int. 2003; 86: 909-915.

[41] Sherma J. Review of HPTLC in drug analysis: 1996-2009. J. AOAC Int. 2010; 93: 754-764.

[42] Jinu John., Ankit Reghuwanshi., Usha K. Aravind., Aravinda kumar, C. T.

Development and validation of a HPTLC method for thedetermination of cholesterol concentration. Journal of food and drug analysis. 2015, 2 3. 219-224.