CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Review Article*

A REVIEW ON ANALYTICAL PROFILE OF SEMAGLUTIDE INPHARMACEUTICAL DOSAGE FORMS AND BIOLOGICAL MATRICES

M. M. Eswarudu[1]*, P. Siva Krishna[1], Shaik Shannu[1], B. Lakshmi Prasanna[1], P. TarunKumar[1], Shaik Afrin[1], Ch. Sujith Kumar[1], P. Srinivasa Babu[2]

[1]Department of Pharmaceutical Analysis, Vignan Pharmacy College, Vadlamudi, 522213, Andhra Pradesh, India.

[2]Department of Pharmaceutics, Vignan Pharmacy College, Vadlamudi, Guntur District –522213, Andhra Pradesh, India.

Abstract:

The chase to improve the quality of life has stimulated desirable changes in research to design and develop a new drug and enhance its safety and effectiveness. Thus, there is a gradual rise in demand to develop susceptible and specific analytical techniques for newly developed drugs. Thus, analysts are striving very hard to develop new and efficient analytical methods to achieve these targets. Semaglutide was approved by United states Food and Drug administration (USFDA). It comes under antidiabetic agents; it acts by improves the efficiency of incretin function by activating GLP-1 receptors. This review article represents the collection and discussion of various analytical methods available in the literature for the estimation of the Semaglutide in pharmaceutical formulations and biological samples consisting of UV, HPLC, UPLC and hyphenated techniques such as LC-MS, LC-MS/MS. Moreover, we discuss about Semaglutide chemical structure, mechanism of action, and pharmacodynamics/pharmacokinetics properties. The present review can be effectively explored to conduct future analytical investigation for the estimation of Semaglutide.

Keywords: *Semaglutide, Analytical Methods, RP-HPLC, UPLC, LC-MS/MS.*

Corresponding author:

M.M. Eswarudu,

Associate Professor, Dept. of Pharmaceutical Analysis,
Vignan Pharmacy College,
Vadlamudi, 522213, Andhra Pradesh, India.
E-mail: eswarmunnangi@gmail.com

QR code

Please cite this article in press M. M. Eswarudu et al, ***A Review On Analytical Profile Of Semaglutide In Pharmaceutical Dosage Forms And Biological Matrices****, Indo Am. J. P. Sci, 2023; 10 (11).*

INTRODUCTION:

Semaglutide is one of the most potent glucagon-like peptide-1 (GLP-1) receptor agonists to treat type 2 diabetes and obesity, which is available as injectable as well as oral dosage forms. Semaglutide is one of the most potent glucagon-like peptides-1 (GLP-1) receptor agonists to treat type 2 diabetes and obesity, which is available as injectable as well as oral dosage forms. Once-weekly subcutaneous injectable Semaglutide (Ozempic®) was approved by the US Food and Drug Administration (FDA) in 2017 and by the European Medicines Agency (EMA) in 2018 for the treatment of type 2 diabetes. Subsequently, a daily oral tablet of Semaglutide (Rybelsus®) was approved in 2019 by the FDA and in 2020 by EMA. In 2021, the US FDA also approved Semaglutide subcutaneous injection (Wegovy®) for chronic weight management in patients with obesity or overweight, which was the first since 2014[1].

When taken as prescribed, it can help lower blood sugar levels up by stimulating the release of insulin and reducing the production of glucose in the liver. SEM also helps to slow down digestion, which can lead to increased feelings of fullness and potentially aid in weight loss. It's important to use SEM as directed by healthcare provider and alongside a healthy diet and exercise plan. It has a clear, colorless and unpleasant sulfur smell compound with a Pka of 5.4. Chemical formula and molecular weight of SEM is $C_{187}H_{291}N_{45}O_{59}$, 4113.58 g/mol respectively [2].

Pharmacokinetic data of Semaglutide:

Absorption: Oral Semaglutide is co-formulated with the absorption enhancer sodium N-(8- [2-hydroxybenzoyl] amino) caprylate, which facilitates the transcellular absorption of Semaglutide across the gastric mucosa.

Distribution: The average clearance (CL) and volume of distribution (Vss) of Semaglutide were estimated as 0.21 mL/min/kg and 0.10 L/kg, respectively. After SC injection, the plasma concentration of Semaglutide gradually increased, achieved the maximum concentrations in 3–12 hr. and decreased with an average $t_{1/2}$ of 7.22–8.99 h [3-6].

Metabolism: It is more than 99% bound to albumin. Semaglutide is cleaved at the peptide backbone, followed by β-oxidation of the fatty acid chain. Naturally occurring GLP-1 is quickly metabolized by dipeptidyl peptidase-4 (DPP-4) and other enzymes, which is ubiquitousin human tissues [7].

Excretion: Degradation products of Semaglutide are excreted via urine and faeces, implying at least partial involvement of the liver in the elimination of Semaglutide [8].

Storage: Store Semaglutide pens (Wegovy) in the refrigerator (36°F to 46°F [2°C to 8°C]). Before removing the cap, it can be stored or from 46°F to 86°F [8°C to 30°C]) in the original carton for up to 28 days. Do not freeze. Do not use Semaglutide if it has been frozen [8].

Mechanism of action: Insulin secretion (glucose Semaglutide improves the efficiency of incretin function by activating GLP-1 receptors. It acts by numerous mechanisms like augmented - dependent), inhibition of glucagon release and suppressed hepatic gluconeogenesis; thereby reducing both fasting as well as postprandial glucose [9]. Figure 1 andTable 1 represents the MOA and list of available marketed formulations of Semaglutide [10-13].

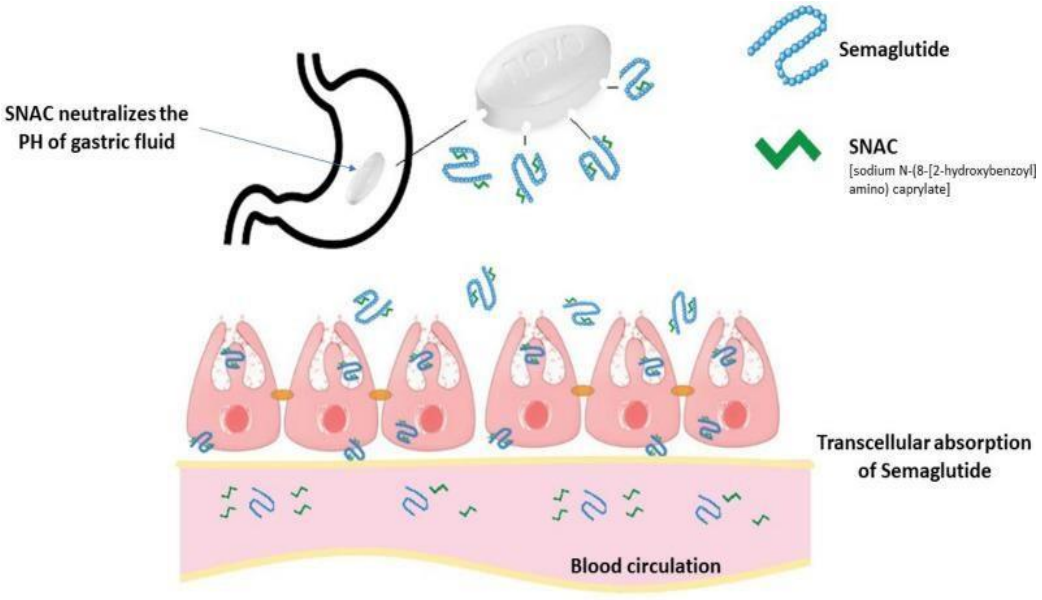

Figure 1: Mechanism of action of Semaglutide

Table 1: Available marketed formulations

S. No.	Trade name	Formulation	Dosage strength	Manufacturer
1	Ozempic	Injection	0.5 mg, 1 mg, 2 mg	Novo Nordisk
2	Wegovy	Injection	1.7 mg, 2.4 mg	Novo Nordisk & Thermos Fisher
3	Rybelsus	Tablets	3 mg,7 mg,14 mg	Novo Nordisk India Pvt Ltd.

Table 2: Reported UV spectrophotometric method for the estimation of Semaglutide

S. No.	Method	Solvent	Wavelength (nm)	Linearity (µg/mL)	LOD (µg/mL)	LOQ (µg/mL)	Assay(%)	Ref.No.
1	UV method	0.01N potassium dihydrogen phosphate	239.80	1-15	0.01	0.03	99.8-102	14
		0.01N potassium dihydrogen phosphate	258.28	1-15	0.26	0.78	99.8-102	
		Sodium acetate buffer PH-5	293.20	1-15	0.03	0.09	98-100.8	
		Sodium acetate buffer PH-5	254.27	1-15	0.13	0.42	98-100.8	

Table 3: RP-HPLC, RP-UPLC and LC-MS Methods for Semaglutide

S. No.	Method	Column type	Mobile phase	Wavelength (nm)	Flow Rate (mL/min)	Run Time (min)	RT (min)	Linearity (µg/mL)	LOD (µg/mL)	LOQ (µg/mL)	Assay(%)	Ref.
1	M1: UV M2: HPLCM3: UPLC	M2: Kromasil18 Column M3: Acquity BEH-C18 (1.7 µ, 100×2.1mm)	0.01Npotassium dihydrogen orthophosphate: Acetonitrile (61:39)	230	M2: 0.9 M3: 0.5	M2: 5.0 M3: 1.2	M2: 2.581 M3: 0.89	1.5-9.0	M1: 0.2 M2: 0.19 M3: 0.07	M1: 0.61 M2: 0.57 M3: 0.24	M1:99.15 % w/v, M2:99.99 % w/v and M3: 100.2% w/v	15
2	RP-HPLC	C18 column (4.6 x 250 mm)	Phosphate buffer pH 4.0: ACN (30:70 % v/v).	254	1	6	2.507	20-100.0	2.535	2.533	102.5	16
3	RP-HPLC	Azilent C18 column (150 x 4.6 x 5 µm)	0.01Npotassium dihydrogen orthophosphate: Acetonitrile (61:39)	230	1	5	2.222	7-48	0.00	0.022	99.99	17
4	RP-HPLC	Inertsil -ODS C18(250 x 4.6 mm, 5 µ)	Methanol: Water in the ratio 70:30	274	1	5	3.237	25.0-150.0	0.57	1.74	98.65	18
5	RP-UPLC	BEH-C18 (50nm × 1.6mm) 1.8µm	0.01Npotassium dihydrogen orthophosphate(3.2pH): Acetonitrile (60:40)	292	0.4	2	1.026	12.5-75.0	0.086	0.261	99.06-100.09	19
6	RP-UPLC	Acquity BEH-C18 (1.7 µ, 100×2.1mm)	0.01Npotassium dihydrogen orthophosphate: Acetonitrile (60:40)	230	0.5	1.2	0.89	1.5-9.0	-	-	98-102	20
7	LC-MS Method	Qtrap 6500+mass spectrometer (Sciex). Liraglutide as an internal standard.	Gradient elution, 0.1% formic acid in water and acetonitrile	The most abundant precursor ion in the Q1 mass scan spectrum was [M + 4H]4+ at m/z 1029.3.		Intra- and inter-day accuracy ranged 89.20–109.50 % in the plasma and 92.00–105.00 % in the brain.		Precision was within 8.92 % in the plasma and 7.94 % in the brain.		0.5 ng/mL	-	21

CONCLUSION:

The present review provides a summary of various analytical methods reported in the literature for the determination of Semaglutide in bulk, pharmaceutical formulations and also in various biological matrices like blood plasma and urine. Analytical methods consisting of chromatography, hyphenated techniques, were employed for determination Semaglutide. From this survey, it is revealed that a handful of analytical methods are obtainable on UV, RP-HPLC, RP-UPLC and only one article was available based on hyphenated methods (LC-MS/MS). The reported data for analysis of Semaglutide revealed that HPLC with UV detection is the most frequent technique employed for the determination of Semaglutide in pharmaceutical dosage forms. For analysis of Semaglutide in biological matrices like blood plasma, urine LC-MS with MS detection is appropriate since this strategy gives precise outcomes and minimal effort. Furthermore, employing MS techniques in LC offered unique selectivity and sensitivity as well as a choice of method for analysis of Semaglutide and its metabolites in biological samples. This review will be useful in further development of the analytical methods for the Semaglutide estimation and also gives a glimpse of the drug Profile.

ACKNOWLEDGEMENTS:

The authors are thankful to Vignan Pharmacy College, Vadlamudi, for providing all necessary facilities for carrying out this review work.

CONFLICTS OF INTEREST STATEMENT:

All the authors declare that they do not have any conflicts of interest.

REFERENCES:

1. Tae Suk Lee, Eun Ji Park, Minkyu Choi, Hyun Seok Oh, Yejin An, Taehyung Kim, Tae Hwan Kim, Beom Soo Shin, Soo young Shin, Novel LC-MS/MS analysis of the GLP-1 analogue Semaglutide with its application to pharmacokinetics and brain distribution studies in rats, Journal of chromatography B, 2023;1221:1-6.
2. https://pubchem.ncbi.nlm.nih.gov/compound/Semaglutide#section=Computed-Properties last accessed on 9th November,2023.
3. Buckley, Stephen T., et al. Transcellular stomach absorption of a derivatized glucagon-like peptide-1 receptor agonist. Science translational medicine.2018;1(467): 10.1126/scitranslmed. aar7047.
4. Knudsen LB, Lau J. The discovery and development of liraglutide and Semaglutide. Frontiers in endocrinology. 2019 Apr 12;10: 155.
5. Jensen, Lene, et al. Absorption, metabolism and excretion of the GLP-1 analogue Semaglutide in humans and nonclinical species. European Journal of Pharmaceutical Sciences 104 (2017): 31-41.
6. https://en.wikipedia.org/w/index.php?title=Semaglutide&oldid=1165483040 accessed on November 9, 2023.
7. Blundell J, Finlayson G, Axelsen M, Flint A, Gibbons C, Kvist T, Hjerpsted JB. Effects of once-weekly Semaglutide on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity. Diabetes Obese Metab. 2017 Sep;19(9):1242-1251. doi: 10.1111/dom.12932.
8. Sanjay Karla, Rakesh Sahay, A Review on Semaglutide: An Oral Glucagon-Like Peptide 1 Receptor Agonist in Management of Type 2 Diabetes Mellitus, Diabetes Ther (2020)11:1965-1982.
9. Paul May, Semaglutide: The Diabetic drug that might also be a cure for obesity, Molecule of the Month, 2021.
10. https://www.ozempic.com/why-ozempic/what-is-ozempic.html accessed on November 9,2023
11. https://www.rybelsus.com/ accessed on November 9, 2023
12. https://www.wegovy.com/ accessed on November 9, 2023
13. https://www.1mg.com/search/all?name=semaglutide accessed on November 9,2023
14. Merugu Manasa, Vijey Aanandhi M, Stability Indicating UV Spectroscopy Method Development Validation and Dissolution Testing of Semaglutide, Journal of Pharmaceutical Negative Results. 2022; 13(4): 1459-146.

15. Manasa M, Vijey Aanandhi M. Stability Indicating Spectroscopic and Chromatographic Estimation of Semaglutide. Turkish Online Journal of Qualitative Inquiry. 2021;12(10): 756-4765.
16. Joshna Sree, Meena, Sivagami, Chandrasekar, Niranjan Babu, A Quantitative RP-HPLC Approach for the Method Development and Validation for the Simultaneous Quantification of Semaglutide and Liraglutide in Pharmaceutical Dosage Forms Journal of Xi'an Shiyou University, Natural Science Edition, 2022;18(11): 684-693.
17. Manasa Merugu, Aanandhi Vijey M, Stability indicating method development and validation of Semaglutide by RP-HPLC in pharmaceutical substance and pharmaceutical product Research Journal of Pharmacy and Technology 2021;14(3):1385-1389, DO:10.5958/0974-360X.2021.00247.
18. Varsha P, Rasapelly Ramesh Kumar, A. Mallik, N. Jyothi, Method development and validation Of Semaglutide Using RP-HPLC, International Journal of Pharmaceutical Research and Applications, 2021;6(5): 434-446.
19. Subha Harika Penmetsa & Raja Sundararajan, Method development and validation of RP-UPLC method for the determination of Semaglutide in bulk and pharmaceutical dosage form, IJRAR- International Journal of Research and Analytical Reviews Research. 2018;5(4): 534-543.
20. Merugu Manasa, Vijey Anandhi M, Stability Indicating RP-UPLC Method Validation and Dissociation Testing of Semaglutide, Journal of Pharmaceutical Negative Results, 2022; 13(5): 1459-1464.
21. Tae Suk Lee, Eun Ji Park, Minkyu Choi, Hyun Seok Oh, Yejin An, Taehyung Kim, Tae Hwan Kim, Beom Soo Shin, Soo young Shin, Novel LC-MS/MS analysis of the GLP-1 analogue Semaglutide with its application to pharmacokinetics and brain distribution studies in rats, Journal of chromatography B, 2023;1221:1-6.