WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Analytical Review of Semaglutide

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ABSTRACT

The study's major goal was to design and verify a simple, precise, and accurate UV-Visible spectrophotometric technique for determining semaglutide in bulk and pharmaceutical dose form. The semaglutide technique was developed utilising a Shimadzu 1800 UV Visible Spectrophotometer and a pair of 10mm path length matched quartz cells. The solutions were scanned at a medium scanning speed in the 200-400 nm range. All parameters, including linearity, accuracy, precision, limit of detection, and limit of quantification, were chosen in accordance with ICH principles and statistically confirmed. Method A was carried out using 0.01N potassium dihydrogen ortho phosphate, whereas Method B was carried out using sodium acetate buffer (pH 5). The maximal absorption of semaglutide was shown to be293nm is the wavelength. Over a concentration range of 1-15g/ml, the medication obeyed Beer-rule. Lambert's The recovery studies' accuracy was determined to be 99.8% - 102% for technique A and 98% - 100.8% for method B. This approach may be used on a regular basis to analyse semaglutide in bulk and pharmaceutical dose form.

Key Words: Semaglutide, Zero order, First-order, UV spectroscopy.

INTRODUCTION

The process of designing an appropriate assay procedure to determine the composition and ensuring that an analytical method is suitable for usage in a laboratory is known as method development. Protocols and acceptance criteria must be used to build analytical techniques [Ashish et al, 2015]. Validation is the process of creating documentation proof that a technique, process, or activity performed in testing and then production maintains the intended degree of compliance at all stages [Lavanya et al., 2013]. It is employed in attaining the quality and safety of the final product mainly in pharmaceutical business [Sibel, 2018].

The medication semaglutide is a once-daily glucagon-like peptide-1 analogue that differs to others by the inclusion of an acyl group with a steric diacid at Lys26. Itis a big synthetic spacer that has been changed by the inclusion of aminobutyric acid at position 8, which provides stability against dipeptidylpeptidase-4. [Gotfredsen and colleagues, 2014]. Semaglutide's IUPAC designation is polypeptide derivatives linked between indole and imidazole derivative. It decreases blood glucose levels by stimulating insulin production while decreasing glucagon secretion [Hjerpsted et al, 2018]. As an addition to diet and exercise, it is advised to enhance glycemic control in persons with type 2 diabetes mellitus [Hjerpsted et al, 2018]. In clinical studies, a decrease in glycated haemoglobin (HbA1c) was shown when compared to other drugs such as sitagliptin, exenatide, and insulin glargine U100. The HbA1c protein is a classic marker of elevated glucose because haemoglobin develops under normal circumstances. 1-deoxyfructose This decreases body weight. The stability of semaglutide via acylation facilitates high- affinity albumin binding and affords a long plasma half-life which allows the once daily dosing [Hjerpsted et al, 2018]. However, no study has been described in the literature on a UV spectrophotometric approach for the measurement of semaglutide utilising 0.01N potassium dihydrogen ortho phosphate and sodium acetate buffer pH-5 as solvent. As a result, the primary goal of this work was to develop and verify a UV spectroscopic technique for determining semaglutide in bulk and pharmaceutical dose form.

METHODS AND MATERIALS

Reagents and chemicals

Novo Nordisk commercialised semaglutide under the brand name ozempic, which was received as a gift sample from Spectrum pharma research solutions in Hyderabad, India. Thermo Fischer Scientific India Private Limited supplied the acetonitrile. All of the chemicals utilised were of the highest analytical quality. A local pharmacy provided the pill formulations.

Instrumentation

For the investigation, a UV 1800 double beam UV Visible Spectrophotometer (shimadzu) with a pair of 10mm path length matched quartz cells was employed. UV solutions 2.42 software was employed. Shimadzu was a brand of electronic balance used for weighing. Volumetric flasks and pipettes used in the investigation were of borosilicate glass. Microsoft Excel was used to do all statistical computations.

SOLUTION PREPARATION

Stock solution preparation

In a 10ml volumetric flask, weigh 10mg of semaglutide and dissolve it in 10ml of buffer:acetonitrile (5:5). For 10 minutes, the solution was sonicated. The wavelength of maximum absorption was determined by scanning the prepared standard solution between 200 and 400 nm.

Making a functioning standard solution

1ml of stock solution was transferred to a volumetric flask of 10ml. The solution was then diluted using a 5:5 acetonitrile:water combination to make a volume of 10ml (working standard solution of 100g/ml).

0.01N potassium dihydrogen ortho phosphate preparation

In a 1000 ml volumetric flask, accurately weigh 1.36 grammes potassium dihydrogen ortho phosphate. 900 ml milli-q water was added to it. and sonicated. The volume was then made up with water until the mark was reached.

Sodium acetate buffer preparation (pH-5)

13.6 gramme sodium acetate and 6 ml glacial acetic acid were dissolved in enough water to form a volume of 1000 ml. If required, the pH was adjusted to 5. VALIDATION OF METHOD

The technique was validated using ICH criteria to evaluate the analyte's linearity, accuracy, precision, LOD, and LOQ [Gilmartin and Gingrich, 2018].

Linearity

The suggested method's linearity was determined by plotting concentration against matching absorbance [Mohammad et al, 2015]. A standard stock solution was further diluted with buffers to create 1µg/ml - 15µg/ml solutions. The calibration curve was created by graphing absorbance versus concentration and then doing a linear regression analysis to produce the linear equation [Acharjya et al, 2010].

Precision

The repeatability (intraday) and intermediate precision (interday) of the assay were used to evaluate precision, which was expressed as % relative standard deviation (%RSD) [Choudhari et al, 2011].

Standard stock solutions (0.05 mL, 0.1 mL, and 0.15 mL) were used in the experiment. The final volume was produced up to the mark using buffer in a 10 ml volumetric flask. The absorbances of these solutions were Precision within one day

tested and recorded separately three times in a day [Shrinivas and Revanasiddappa, 2015].

Inter-day accuracy

In 10 ml volumetric flasks, standard stock solutions (0.05 ml, 0.1 ml, and 0.15 ml) were taken and volume was brought up to the mark with buffer. The absorbances of these solutions were tested and recorded three times in three days. Accuracy

The approach's accuracy was measured using the usual addition recovery method at three distinct levels: 50%, 100%, and 150%. A known amount of standard medication was administered to tablet samples at three distinct concentration levels in this study [Arora et al, 2011]. The absorbance was measured. and% recovery were computed.

Limits of detection and quantification

The limits of detection (LOD) and quantification (LOQ) were calculated using the standard deviation of response and the slope of the corresponding curve using the following equations: 3.3 / S (LOD) and 10 / S (LOQ) [Argekar and Sawant, 1999].

Semaglutide tablet testing

This approach was used to examine a commercially available formulation of semaglutide. An quantity of semaglutide (injection) corresponding to 10mg/ml was transferred to a 100ml volumetric flask, and the contents of the flask were dissolved in 50 ml of buffer and ultra sonicated for 10 minutes. The solution was filtered, and the final volume was increased to 100 ml with the same solvent to get a stock solution containing 100g/ml of semaglutide. After suitable dilutions, the absorbance was measured, and the concentration of each analyte was calculated using the calibration curve formulae.

Important Administration Requirements

• Before starting WEGOVY, teach patients appropriate injection technique. Complete administration instructions with images may be found in the accompanying Instructions for Use.

· Visually inspect WEGOVY before each injection. Only use if the solution is clear, colourless, and free of particles.

WEB ADMINISTRATIONS ARE AVAILABLE ON THE WEB.

- WEGOVY should be administered subcutaneously in the belly, thigh, or upper arm. The time of day and location of injection can be varied without affecting the dosage.
- If a dosage is missed and the next regular dose is more than 2 days (48 hours) away, take WEGOVY as soon as feasible. If you miss one dosage and the next planned dose is less thanDo not deliver the dosage for two days (48 hours). • If more than two consecutive doses are missed, restart dosing as planned or, if necessary, reinitiate WEGOVY and follow the dosage escalation schedule, which may prevent the likelihood of gastrointestinal problems associated with reinitiation of therapy.

2.3 Recommended Dosage •

Initiate WEGOVY with a dosage of 0.25 mg injected subcutaneously once-weekly and follow the dose escalation strategy in Table 2 to reduce gastrointestinal adverse events [see Adverse Reactions (6.1)].

Table 2. Dose Escalation Schedule

Weeks	**Weekly Dose**	
1 through 4	0.25 mg	Dose escalation
5 through 8	0.5 mg	
9 through 12	1 mg	
13 through 16	1.7 mg	
Week 17 and onward	2.4 mg	Maintenance dose

- Consider postponing dosage escalation for 4 weeks if patients do not tolerate a dose during dose escalation.
- WEGOVY's maintenance dosage is 2.4 mg administered subcutaneously once a week.
- If patients do not tolerate the 2.4 mg once-weekly maintenance dosage, it can be temporarily reduced to 1.7 mg once-weekly for a maximum of 4 weeks. After four weeks, raise WEGOVY to the maintenance dose of 2.4 mg once a week. If the patient is unable to tolerate the 2.4 mg dosage, discontinue WEGOVY.
- Monitor blood glucose levels in individuals with type 2 diabetes before and throughout WEGOVY medication.

DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution available in 5 pre-filled, disposable, single-dose pens:

Dose per Injection	**Total Strength per Total Volume**
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg / 0.75 mL
2.4 mg	2.4 mg / 0.75 mL

CONTRAINDICATIONS

WEGOVY is not recommended in the following situations:

- A personal or family history of medullary thyroid cancer (MTC) or Multiple Endocrine Neoplasia type 2 (MEN 2) [see Warnings and Precautions (5.1)].
- A previous severe hypersensitivity reaction to semaglutide or any of WEGOVY's excipients. Semaglutide has been linked to severe hypersensitivity responses such as anaphylaxis and angioedema [see Warnings and Precautions (5.6)].

5. CAUTIONS AND WARNINGS

5.1 Thyroid C-Cell Tumor Risk

After lifetime exposure to clinically relevant plasma levels, semaglutide induced a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell cancers (adenomas and carcinomas) in mice and rats [see Nonclinical Toxicology (13.1)]. WEGOVY is not known to produce thyroid C-cell malignancies, including medullary thyroid carcinoma (MTC), in humans. The human significance of semaglutide-induced mouse thyroid C-cell malignancies is unknown.

In the postmarketing era, cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been described; the data in these studies are insufficient to prove or reject a causal link between MTC and GLP-1 receptor agonist usage in humans.

WEGOVY is not recommended for people who have a personal or family history of MTC or who have MEN 2. Inform patients about the potential risk of MTC associated with the use of WEGOVY and the symptoms of thyroid tumours (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine serum calcitonin monitoring or use of thyroid ultrasonography for early identification of MTC is of unclear usefulness. WEGOVY was used to treat patients. Because of the limited test specificity for serum calcitonin and the high background frequency of thyroid illness, such surveillance may raise the risk of needless operations. Serum calcitonin levels that are significantly increased may suggest MTC, and individuals with MTC often have calcitonin levels greater than 50 ng/L. If serum calcitonin is discovered to be high, the patient should be investigated further. Patients who have thyroid nodules on physical examination or neck imaging should be investigated further.

5.2 Pancreatitis Acute

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been reported in individuals using GLP-1 receptor agonists such as semaglutide. In clinical studies, people treated with WEGOVY had acute pancreatitis [see Adverse Reactions (6)]. Following the initializationWEGOVY, closely monitor patients for signs and symptoms of acute pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting). If acute pancreatitis is detected, WEGOVY should be stopped immediately and proper therapy should begin. WEGOVY should not be continued if acute pancreatitis is proven.

WEGOVY has not been examined in people who have had pancreatitis in the past. It is uncertain whether people with a history of pancreatitis are more likely to develop pancreatitis on WEGOVY.

Acute Gallbladder Disease (5.3)

Cholelithiasis was reported by 1.6% of WEGOVY-treated patients and 0.7% of placebo-treated individuals in WEGOVY randomised clinical studies. 0.6% of WEGOVY-treated patients and 0.2% of placebo-treated individuals had cholecystitis. Significant or quick weight loss can raise the risk of cholelithiasis; nevertheless, even after accounting for the degree of weight loss, the incidence of acute gallbladder illness was higher in WEGOVY-treated individuals than in placebo-treated patients. Gallbladder investigations and proper clinical follow-up are recommended if cholelithiasis is suspected.

Hypoglycemia (low blood sugar)

WEGOVY reduces blood glucose levels and can result in hypoglycemia.

Hypoglycemia (defined as plasma glucose less than 54 mg/dL) was recorded in 6.2% of WEGOVY-treated patients versus 2.5% of placebo-treated individuals in a study of patients with type 2 diabetes and BMI higher than or equal to 27 kg/m2. One WEGOVY-treated patient had severe hypoglycemia (requiring the aid of another person), but no placebo-treated individuals did.

Patients suffering with type 2 diabetesWEGOVY may increase the risk of hypoglycemia, particularly severe hypoglycemia, when used with an insulin secretagogue (e.g., sulfonylurea) or insulin [see Adverse Reactions (6.1)]. Patients treated with semaglutide at dosages of 0.5 and 1 mg in conjunction with insulin experienced hypoglycemia. The inclusion of WEGOVY in insulin-treated individuals has not been studied.

Inform patients about the danger of hypoglycemia and teach them about the symptoms of hypoglycemia. Monitor blood glucose levels in individuals with type 2 diabetes before and throughout WEGOVY medication. Consider lowering the dose of a concomitantly given insulin secretagogue (such as sulfonylureas) or insulin while starting WEGOVY to lessen the risk of hypoglycemia [see Drug Interactions (7)].

There is an acute kidney injury.

There have been postmarketing reports of acute kidney damage and worsening chronic renal failure in individuals treated with semaglutide, requiring hemodialysis in some cases. Although individuals with renal impairment are more likely to experience acute kidney damage, some of these occurrences have been described in patients with no known underlying renal illness. The majority of reported occurrences occurred in individuals who had nausea, vomiting, or diarrhoea, which resulted in volume depletion [see Adverse Reactions (6)].

When starting or increasing WEGOVY dosages in patients who have experienced significant adverse gastrointestinal events, keep renal function in mind. In patients with renal impairment, monitor renal function and record any adverse events that might lead to volume depletion.

5.6 Excessive sensitivity

There have been reports of severe hypersensitivity responses (e.g., anaphylaxis, angioedema). Using semaglutide. If hypersensitivity responses occur, stop using WEGOVY immediately, treat according to standard of care, and monitor until signs and symptoms diminish. Use with caution in individuals who have previously demonstrated hypersensitivity to semaglutide or any of the excipients in WEGOVY [see Contraindications (4)].

Other GLP-1 receptor agonists have been linked to anaphylaxis and angioedema. If a patient has a history of anaphylaxis or angioedema with another GLP-1 receptor agonist, take cautious because it is uncertain if they would be prone to similar problems with WEGOVY.

Diabetic Retinopathy Complications in Type 2 Diabetes Patients

Diabetic retinopathy was observed by 4.0% of WEGOVY-treated individuals in a study of patients with type 2 diabetes and a BMI more than or equal to 27 kg/m2. 2.7% of patients were given a placebo.

Diabetic retinal complications (a 4-component adjudicated outcome) occurred in individuals treated with semaglutide injection (3.0%) compared to placebo (1.8%) in a 2-year study with semaglutide 0.5 mg and 1 mg once-weekly injection in patients with type 2 diabetes and high cardiovascular risk. Individuals having a history of diabetic retinopathy at baseline had a higher absolute risk increase for diabetic retinal complications (semaglutide injection 8.2%, placebo 5.2%) than patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%).

Rapid glucose control improvement has been linked to a transitory exacerbation of diabetic retinopathy. Long-term glycemic management with semaglutide has not been evaluated in terms of diabetic retinopathy consequences. Patients who have had diabetic retinopathy in the pastDiabetic retinopathy should be evaluated for progression.

5.8 Increase in Heart Rate

In clinical studies, WEGOVY-treated individuals had mean increases in resting heart rate of 1 to 4 beats per minute (bpm) compared to placebo. When compared to placebo, more patients treated with WEGOVY had maximum changes from baseline at any visit of 10 to 19 bpm (41% against 34%, respectively) and 20 bpm or more (26% versus 16%, respectively).

Monitor heart rate at regular intervals in accordance with standard clinical practise. Instruct individuals to notify their healthcare providers if they have palpitations or a racing heartbeat while resting during WEGOVY therapy. WEGOVY should be discontinued if individuals report a prolonged rise in resting heart rate.

5.9 Suicidal Behavior and Thoughts

Suicidal behaviour and thoughts have increased. Clinical studies with additional weight control drugs have also been described. Patients on WEGOVY should be monitored for the development or worsening of depression, suicidal thoughts or behaviour, and/or other unexpected changes in mood or behaviour. WEGOVY should be stopped in patients who have suicidal thoughts or actions. The purpose of this article is to raise awareness of the dangers of using alcohol.

RESULTS AND DEBATE

The new technique was verified in terms of linearity, accuracy, precision, LOD, and LOQ using ICH criteria. The standard solution was individually scanned, and semaglutide spectra were collected between 200 and 400 nm. The maximum of semaglutide was found to lie at 293.80nm for 0.01N potassium dihydrogen ortho phosphate (method A) and 293.20nm for sodium acetate (method B). The first layerThe order derivative spectrum of semaglutide at various concentrations was discovered to be 240.55 (method A), 254.27 (method B) for maxima and 254.28 (method A), 213.45 (method B) for minima. Figure 5-8 depicts the overlain spectrum as well as a summary of validation parameters.

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