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Summary of chromatographic analysis methods of anti diabetic gliflozins Empagliflozin, Canagliflozin and Dapagliflozin

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Keywords

Review;

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SGLT-2

Abstract

Sodium glucose co-transporter-2 (SGLT-2) inhibitors are relatively new developed effective oral anti-diabetic agents used in treatment of type 2 Diabetes Mellitus. They present either alone or in combination with other ant diabetic agents such as linagliptin, Saxagliptin and metformin. Therefore, the necessity to explore and compare the existing analytical and bioanalytical assays used for determination of such drugs either single or in combination is crucial. Many methods were reported in the literature for the bio-analysis and analysis of three novel gliflozins with applying the method on different dosage forms and different chemical and biological samples. Furthermore, this review offered an overview of different methods used for determination of every drug alone in a tabulated comparative way. Moreover, the present review emphasized the most common stability indicating assays to be of interest to the analysts in the area of drug control.

Introduction

Around the world, about 382 million patients are suffering from diabetes mellitus ⁽¹⁾. Global burden of disease study in 2010 shows that morbidity rate related to diabetes mellitus is doubled just in years from 1990 to 2010, also an increase with 30% in DALYs (disability adjusted life years) ⁽²⁻⁴⁾. Other studies shows that diabetes mellitus patients will reach almost 600 million by the year of 2035 ⁽¹⁾. These forecast seems to be unobtrusive especially with estimated nearly 300 million people has impaired glucose tolerance ⁽⁵⁾. Global burden of Diabetes mellitus is much higher in developing countries rather than the developed ones. About 80% of persons with diabetes mellitus living currently in communities with low- to middle-income. Middle East and Asia are considered the regions with the hardest-hit.⁽¹⁾.

Dapagliflozin (DG) and empagliflozin (EG), and canagliflozin (CG) (Fig.1) are phlorizin derivatives, approved by FDA for use in people with type 2 diabetes that inhibit sodium-glucose co-transporter-2 (SGLT2) and thereby reduce renal tubular glucose reabsorption and hence blood glucose concentrations by promoting urinary glucose excretion.

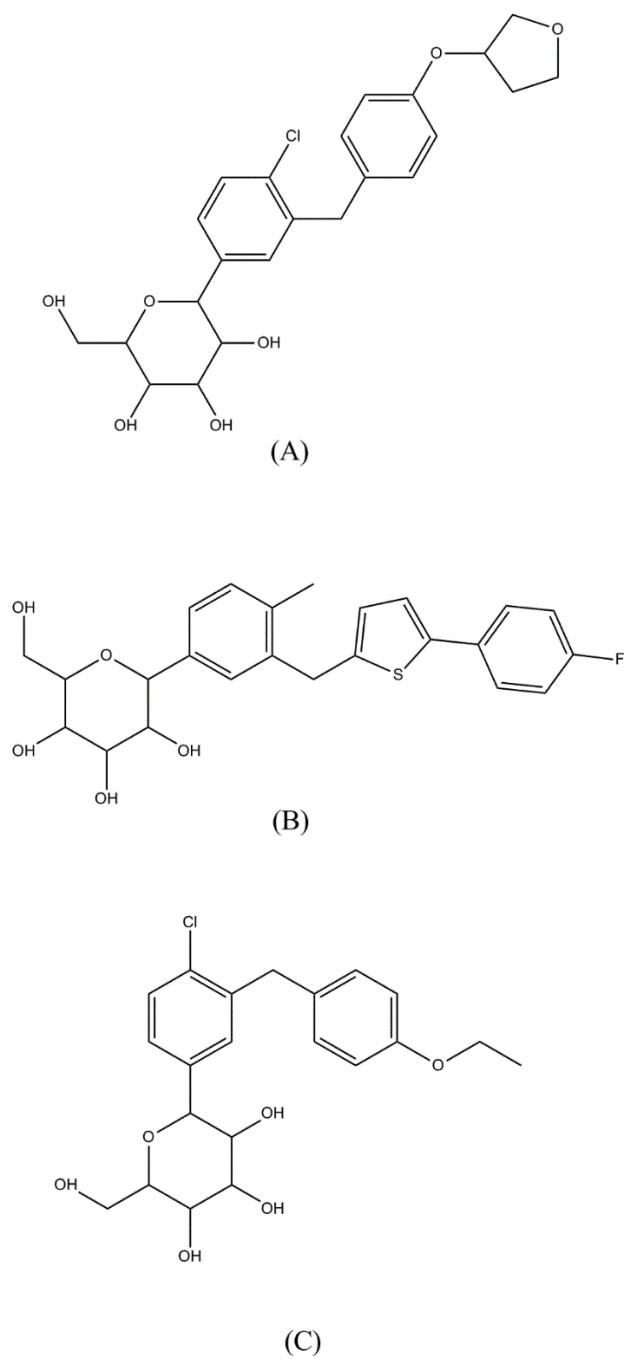


Figure (1): Chemical structures of empagliflozin (A), canagliflozin (B) and dapagliflozin (C).

Table (1): Chromatographic methods for analysis of empagliflozin either in bulk, dosage form or biological fluids.

Stationary phase	Mobile phase	Application	Detection
C ₁₈ column	phosphate buffer (pH 3): methanol, (30:70 v/v)	Tablet	UV 240 nm ⁽¹⁴⁾
C ₁₈ column	Deionized water and acetonitrile in the ratio of (10:90, v/v)	Human plasma	MS/MS ⁽¹⁵⁾
C ₁₈ column	Acetonitrile - water (75: 25, v/v)	Tablet impurities	MS/MS ⁽¹⁶⁾
C ₁₈ column	phosphate buffer (pH 4.8), acetonitrile, methanol (15:80:5, v/v/v)	Tablet	UV 227 nm ⁽¹⁷⁾
C ₁₈ column	0.1% formic acid: acetonitrile, (50:50, v/v)	Human plasma	MS/MS ⁽¹⁸⁾
C ₈ column	0.1 OPA: Acetonitrile, (70:30, v/v)	Tablet	UV 233 nm ⁽¹⁹⁾
C ₁₈ column	potassium dihydrogen phosphate buffer pH (4)- methanol (50 : 50, v/v)	Tablet	UV 225 nm ⁽²⁰⁾
C ₁₈ column	0.1% aqueous formic acid: acetonitrile, 75:25, v/v	Tablet	MS/MS ⁽²¹⁾

Table (2): Chromatographic methods for analysis of Dapagliflozin either in bulk, dosage form or biological fluids.

Stationary phase	Mobile phase	Application	Detection
C ₁₈ column	Acetonitrile : Ortho phosphoric acid the (55:45, v/v)	Bulk	UV at 203 nm ⁽²²⁾
C ₁₈ column	Ortho phosphoric acid : acetonitrile (pH 4.5) (45:55 v/v)	Bulk	UV at 245 nm ⁽²³⁾
C ₁₈ column	Phosphate Buffer: methanol: acetonitrile (pH 6.5) (50:30:20 v/v/v)	Tablet	UV at 240 nm ⁽²⁴⁾
C ₁₈ column	Triethylamine: acetonitrile pH (6.8) (50:50, v/v)	Tablet	UV at 240 nm ⁽²⁵⁾
C ₁₈ column	acetonitrile: di-potassium hydrogen phosphate (pH 6.5) (40:60 v/v)	Tablet	UV at 222 nm ⁽²⁶⁾
C ₁₈ column	Water: acetonitrile (60/40 v/v).	Rat plasma	MS/MS ⁽²⁷⁾

Table (3): Chromatographic methods for analysis of Canagliflozin either in bulk, dosage form or biological fluids.

Stationary phase	Mobile phase	Application	Detection
C ₁₈ column	Ammonium acetate: acetonitrile (pH 3.5) (65:35, v/v)	Tablet	UV at 254 nm ⁽²⁸⁾
C ₁₈ column	Phosphate buffer : acetonitrile (pH 4.5) (65:35, v/v)	Tablet	UV at 248 nm ⁽²⁹⁾
C ₁₈ column	Phosphate buffer : acetonitrile (pH 4.5) (53:47, v/v)	Tablet	UV at 240 nm ⁽³⁰⁾
C ₁₈ column	Phosphate buffer : Acetonitrile : methanol (pH 4.5) (40:40:20, v/v)	Tablet	UV at 212 nm ⁽³¹⁾
C ₁₈ column	20 mM potassium dihydrogen orthophosphate : acetonitrile (pH 3.2) (45 : 55, v/v)	Human Plasma	Fluorescence detection at 280 and 325 nm (excitation and emission) ⁽³²⁾
C ₈ column	36.46 mM Acetate buffer : acetonitrile : methanol(pH 4.5) (30:50:20, v/v)	Human Plasma	UV at 290 nm ⁽³³⁾
C ₁₈ column	0.05% v/v Triethylamine : Acetonitrile (pH 6.5) (45:55, v/v)	Tablet	UV at 215 nm ⁽³⁴⁾
C ₁₈ column	Acetonitrile : Ammonium acetate buffer (pH 4.5) (45:55, v/v)	Tablet	UV at 252 nm ⁽³⁵⁾
C ₁₈ column	Acetonitrile: water (80:20,v/v)	Rat plasma	MS/MS ⁽³⁶⁾
C ₁₈ column	Acetonitrile: 0.1% formic acid (90:10, v/v)	Rat plasma	MS/MS ⁽³⁷⁾

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