الايه

بسم الله الرحمن الرحيم

(ربي اوزعني ان اشكر نعمتك التي انعمت علي وعلى والدي وان اعمل صالحا ترضاه وادخلني في رحمتك مع عبادك الصالحين)

النمل الايه 19

Dedication

To the candle that burn to light my way my Dear Father

To the great woman who stay awoke at night to draw the happiness

in my life my Dear Mother.

To my brothers and sister.

Acknowledgements

First of all praise and thanks be to Allah, the lord of the universe who gave me patience to accomplish this great work.

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Abstract

In this work simple, precise and accurate spectrophotometric and high performance liquid chromatography (HPLC) assay methods for spironolactone in raw material and tablet dosage form were developed and validated. HPLC analysis method was developed using inertstil C_{18} (250 *4.6 mm), 5µm column with a mobile phase consisting of phosphate buffer solution pH = 4 and acetonitrile in (1:1) ratio. The flow rate was adjusted at 1.5 ml/min, detection wavelength, at 240 nm, temperature, at 40 ^{o}C and retention time was found to be 4.5 min. In spectrophotometric analytical method, two methods in UV region were developed and validated as Hydrazine and Hydroxylamine methods. The maximum absorption wavelength for determination of spironolactone was found to be 236.8 nm, but those for Hydrazine and Hydroxylamine derivatization were found to be 251.5 nm and 263.7 nm, respectively. Beer's law was obeyed in the concentration range from 20 ppm to 30 ppm for both HPLC and spectrophotometric analysis methods. The assay percentage (mean ±RSD) for tablet commercial formulation was found to be (98.00±0.39) %, (97.15±0.28) % and (98.25±0.59) % for Hydrazine, Hydroxylamine and HPLC methods, respectively. The percentage of recovery was found to be (100.20-102.65) %, (98.47-100.67) % and (99.40-101.99) % for Hydrazine, Hydroxylamine and HPLC methods, respectively. The limit of detection (LOD), however, was found to be in the range from 0.028 ppm to 0.553 ppm for all methods. The limit of quantitation (LOQ) was also found to be in the range from 0.086 ppm to 1.677 ppm for all methods. All the validation methods were carried out according to ICH Q2 (R1) guideline.

المستخلص

الهدف من البحث هو تطوير طريقتين مضوائيتين طيفيتين وطريقه كروماتوغرافيا الضغط عالية الأداء لتعين نسبه spironolactone في المواد الخام وفى جرعات في شكل حبه والتحقق من صلاحيتهم. في طريقه الكروماتوغرافيا عالية الأداء عند استخدام طور متحرك من Acetonitrile و محلول منظم من فوسفات البوتاسيوم ثنائية الهيدروجين بنسبه (1:1) و عمود فصل ذو طول 250 mm وقطر 4.6 mm و حجم حبيبات 5مايكروميتر و عند طول موجي 240 nm وجد أن زمن الاستبقاء spironolactone يساوي 4.5 min. أما في الطريقة المطيافيه تم تطوير والتأكد من صلاحية طريقتين في مدى الاشعه فوق البنفسجية ; طريقة الهيدرازين وطريقه الهيدروكسيلامين. الطول الموجي لل spironolactone هو 236.8 nm , لمشتق الهيدرازين و لمشتق الهيدروكسيل امين هو 251.5 nm و263.7 nm على التوالي. وجد أيضا أن طريقة الكروماتوغرافيا زات الضغط العالي و الطرق الطيفية في مجال الاشعه فوق البنفسجية ذات خطيه في المدى من 20 ppm إلي 30 ppm. نسبة spironolactone في الجرعات في شكل الحبة التجارية (98.00±0.39)% ,(97.15±0.28) % و (98.25±0.59) % لكل من طريق الهيدرازين , طريقه الهيدروكسيلامين وطريقه الكروماتوغرافيا الضغط العالي على التوالي. وكذلك كمية spironolactone المستعادة في المدى في الجرعات في شكل الحبة التجارية (100.20-102.65) % ,(98.47-100.67) % و (99.40-101.99) % لكل من طريقة الهيدرازين , طريقة الهيدروكسيلامين وطريقه الكروماتوغرافيا الضغط العالي على التوالي. و لكن وجد أن حد التعرف (limit of detection) في المدى ppm (-0.028 0.553) وكذلك حد التكمية (limit of quantitation) في المدى ppm (0.086-1.677) لكل الطرق. تم التأكد من صلاحية كل الطرق وفقا لتوجيهات ICH Q2 (R1) .

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List of abbreviations

ICH	International conference on harmonization
QL	Quantitation limit
DL	Detection limit
HPLC	High performance chromatography
UV	Ultra violet
ABS	Absorption
SPI	spironolactone