OPTIMIZATION & CHARACTERIZATION OF GLIPIZIDE ORAL SUSPENSION FORMULATION

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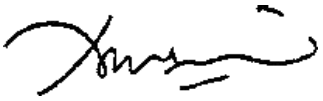
MASTER OF SCIENCE

UNIVERSITI MALAYSIA PAHANG

SUPERVISOR'S DECLARATION

I hereby declare that I have checked this thesis and in my opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Master of Science.



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ABSTRAK

Glipisid adalah ubat anti-diabetes yang tergolong dalam kelas dadah yang dikenali sebagai sulfonylurea. Pengambilan glipisid beserta dengan diet yang seimbang dan senaman yang mencukupi boleh mengawal tahap gula dalam darah pesakit diabetes jenis 2. Glipisid adalah alternatif yang lebih baik untuk metformin sebagai ubat anti-hiperglisemia kerana ia lebih efisien dalam jumlah yang kecil dan tidak memberi kesan sampingan yang ketara. Oleh kerana itu, glipisid telah digunakan untuk membuat larutan dadah anti-hiperglisemia. Dalam larutan glipisid, terdapat parameter seperti kanji asli dan natrium karboksimetil selulosa yang mempengaruhi ciri fizikalnya, kemungkinan parameter tersebut saling mempengaruhi kesan terhadap larutan. Oleh kerana itu, adalah mustahak untuk menggunakan kaedah pengoptimuman yang dapat menilai hubungan antara parameter tersebut, supaya jumlahnya dalam larutan dapat ditentukan untuk menjadikannya sempurna dan optimum. Kaedah Permukaan Respons adalah gabungan kaedah statistik dan matematik yang biasa digunakan dalam industri makanan untuk menilai kesan beberapa faktor dan untuk mengoptimumkan keadaan dan demikian digunakan dalam kajian ini untuk mengoptimumkan pengeluaran larutan glipisid. Dalam kajian ini, parameter yang berkaitan dengan penyediaan larutan seperti kanji asli, natrium KMS dan Polysorbate 80 telah disiasat. Respons yang terlibat adalah kelikatan dan kadar pemendapan. Kaedah Satu Faktor pada Satu Masa telah digunakan untuk mendapatkan julat bagi parameter yang dikaji. Kemudian, menggunakan perisian Pakar Rekaan, julat bagi setiap parameter telah dimasukkan dalam Reka Bentuk Komposit Sentral untuk membuat 20 kombinasi parameter yang berbeza untuk formulasi. Setelah selesai formulasi, nilai kelikatan dan kadar pemendapan yang diperolehi telah dimasukkan dalam Kaedah Permukaan Respons untuk pengoptimuman. Larutan optimum telah dihasilkan dan diuji untuk kadar pemendapan, diameter zarah, kelikatan, pengukuran potensi zeta, pelepasan dadah *in-vitro* dan kestabilan termangkin. Untuk kelikatan, nilai r^2 adalah 0.1633 dan nilai p adalah 0.8510 manakala untuk pemendapan, nilai r^2 adalah 0.0759 dan nilai p adalah 0.9780. Isipadu pemendapan dan kelikatan larutan masing-masing adalah 0.0047462ml dan 0.0039171 Ns/m^2. Nilai potensi zeta ialah -38.63mV. Semasa ujian pelepasan dadah *in-vitro*, peratusan pelepasan dadah adalah sebanyak 98.80% selepas satu jam. Kesimpulannya, parameter seperti kanji asli, natrium KMS dan Polysorbate 80 tidak memberi kesan yang signifikan terhadap larutan. Kajian ini

dapat ditambahbaik dengan menjalankan ujian pelepasan dadah in-vivo serta mengubah bentuk dos kepada nanopartikel. Ujian pelepasan dadah in-vivo akan memberi maklumat terperinci mengenai ciri-ciri larutan.

ABSTRACT

Glipizide is an anti-diabetic medication which belongs to a class of drugs known as sulfonylurea. It is used with a proper diet and exercise program to control high blood sugar in people with type 2 diabetes. Glipizide can be a better alternative for metformin as an anti- hyperglycemic drug as it is more efficient in a smaller amount and imposes lesser side effects. Therefore, glipizide was used to make an anti-hyperglycemic drug suspension. In glipizide suspension, there are parameters like native starch, sodium carboxymethyl cellulose and Polysorbate 80 affecting its physical characteristics. There is a high chance for these parameters to interface and influence each other's effects on the suspension. Hence, it is essential to utilize an optimization method that can quantify the relationship between those two parameters, so that their amount in the suspension can be determined to make it perfect and optimum. Response Surface Methodology (RSM) is a combination of statistical and mathematical methods commonly used in the food industry to quantify the impacts of a few factors and to optimize conditions and thus applied in this study to optimize the production of glipizide suspension. In this study, preparation of suspension with parameters such as sodium CMC, native starch and Polysorbate 80 was investigated. The responses involved were viscosity and sedimentation rate. One Factor at One Time method was used to obtain the ranges for the aforementioned parameters. Then, using Design Expert software, the ranges of the parameters were entered in the Central Composite Design (CCD) to create 20 different combinations of parameters for formulation. After conducting the formulation, the values of viscosity and sedimentation rate obtained were keyed in Response Surface Methodology (RSM) for optimization. An optimum suspension was formulated and tested for sedimentation rate, mean particle diameter, viscosity, zeta potential measurement, *in-vitro* drug release and accelerated stability. Viscosity had an r^2 value of 0.1633 and p value of 0.8510; whereas for sedimentation, r^2 value was 0.0759 and p value was 0.9780. The sedimentation volume and viscosity of suspension are 0.0047462ml and 0.0039171Ns/m^2 respectively. Zeta potential value is -38.63mV. During *in-vitro* drug release studies, the percentage of drug release is 98.80% after an hour. In conclusion, there is no significant effect on suspension due to individual parameters and their interactions. This study can be improvised by including in-vivo drug release study as well as changing the dosage form to nanoparticles. In-vivo drug release test will provide

more information on the characteristics of the suspension whereas nanoparticles dosage form will help to reduce the quantity and toxicity of glipizide as well as increase its safety and efficacy.

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