

**UNIVERSITI TEKNOLOGI MARA**

**SUPERDISINTEGRANT- AND  
EFFERVESCENT AGENT-LESS  
DISPERSIBLE FAST-RELEASE  
TOLBUTAMIDE MATRIX PREPARED  
BY MELT PELLETIZATION  
TECHNIQUE**

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Thesis submitted in fulfillment  
of the requirements for the degree of  
**Master of Science**


**Faculty of Pharmacy**

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## AUTHOR'S DECLARATION

I declare that the work in this thesis/dissertation was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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## ABSTRACT

Solid dispersion utilizing superdisintegrants and effervescent agents was met with slow matrix disaggregation during dissolution and effervescence loss during storage, thereby delaying drug dissolution. This study employed electrolyte as alternative dispersant of fast-release matrix prepared using solvent-free melt pelletization technique which prevented instantaneous reaction between electrolyte and solvent during agglomeration and allowed such reaction to occur only in dissolution phase. The melt pellets were prepared using lactose and polyethylene glycol (PEG) 3000 as hydrophilic carriers, calcium acetate and calcium carbonate as electrolytes, tolbutamide as poorly water-soluble drug in free form and embedded in PEG 3000. These pellets were subjected to drug dissolution and physicochemical tests at molecular scale. The dissolution of tolbutamide in simulated gastric milieu increased following its formulation into pellets due to enhanced drug segregation and amorphization. A further increase in drug dissolution was attainable through pellet formulation with water-soluble calcium acetate instead of effervescent acid-soluble carbonate salt. Calcium acetate dissolved rapidly in aqueous medium to initiate turbulence in core matrix and fast pellet break-up through erosion and disintegration. Small dispersible particles with elevated dissolution surface area were formed and had pellet fast-release characteristics unaffected by prolonged matrix storage for 17 months at 25 °C and 50% relative humidity.

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