# 論文 / 著書情報
# Article / Book Information

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# 論 文 要 旨

THESIS SUMMARY

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| 専攻：<br>Department of | 物質科学　専攻 | 申請学位（専攻分野）：<br>Academic Degree Requested | 博士　（理学）<br>Doctor of |
| 学生氏名：<br>Student's Name | Okky Dwichandra Putra | 指導教員（主）：<br>Academic Advisor(main) | 植草　秀裕 |
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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）


This dissertation has covered the relationships between crystal structure and physicochemical property relationships in multicomponent pharmaceutical. Some study cases were utilized which cover not only designing novel multicomponent crystals but also analyzing the marketed multicomponent crystals. The alterations of physicochemical properties due to the change of the crystal structure of pharmaceutically multicomponent crystals which were used in this study were elucidated for the first time.

The first study case in this dissertation is related with designing a rare drug-drug multicomponent crystal of two antidiabetic drugs which overcome the weaknesses of unfavorable physicochemical properties in each parent drugs. The combination of the non-insulin-dependent diabetes mellitus drugs metformin and gliclazide were used in this part. Despite providing better results regarding glycemic control and the lipid index, which are often major problems during the treatment of diabetes, it has been a reality that both metformin and gliclazide exhibit unfavorable physicochemical properties. The base form of metformin is a hygroscopic powder and gliclazide has poor solubility. It is intetersting that the multidrugs crystal of metformin-gliclazide were present as a non-hygroscopic and soluble powder. The reduced hygroscopicity of the multicomponent crystals as compared with metformin alone could be explained by the crystal structure. In this case, metformin molecules were located in the channel formed by gliclazide molecules; thus, the gliclazide molecules, which were less hydrophilic, protected metformin and formed hydrogen bonds to close potential hydrogen bonding sites. In addition, the multidrugs crystal showed an improvement in solubility and dissolution rate compared to gliclazide. These improvements were related with the existence of channel structures that could play an important role in improving solubility owing to the molecular characteristics of the surface. In this case, we were also able to establish the first method to observe directly the existence of the channel structure in the crystal during solubilization.

The second study case utilized a design and a physicochemical property evaluation of rare isostructural multicomponent gliclazide crystals. The isostructural of antidiabetic gliclazide crystal were formed by hybridization with the aminopyridine derivatives (4-aminopyridine, and 3,4-diaminopyridine). We found that isostructural salts show enhanced dissolution rate relative to their raw material, although the dissolution profile between the salts was slightly different. In this case, the dissolution rate of 4-aminopyridine salt was faster than that of 3,4-diaminopyridine salt. This phenomena was correlated with the lower packing efficiency and lower lattice energy which was represented by melting point difference in 4-aminopyridine salt which turn leads to faster dissolution.

The last study case provided a molecular insight in understanding the physicochemical changes of antibiotic multicomponent crystal of ciprofloxacin hydrochloride during a common manufacturing process of heating. By heating the marketed sesquihydrate crystal of ciprofloxacin hydrochloride, two anhydrous forms were formed (anhydrous form I and II). The dissolution profiles, stability and appearance were evaluated among the phases of ciprofloxacin hydrochloride. The solid-state dehydration mechanism were established from the structural correlation among the phases and the understanding of physicochemical properties was obtained by deriving structural differences among the phases.


備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。
Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1copy of 800 Words (English).