Investigation of dissolution and permeation properties of amorphous drug particles dispersed in wax-based formulations

List Author(s)

Hiromasa Uchiyama[1], Chihiro Sakamoto[1], Yasuhiro Nomoto[1], Akane Shirahama[2], Hideo Takeda[2], Yuichi Tozuka[1]

Author Affiliation/Company

[1] Department of Formulation Design and Pharmaceutical Technology, Faculty of Pharmacy, Osaka Medical and Pharmaceutical University,

4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan

[2] PHYSIO MCKINA Co., Ltd. Saito Bio Innovation Center 2F, Saitoasagi 7-7-20, Ibaraki-Shi, Osaka, 660-0801, Japan

CONTACT INFORMATION: Mail: hiromasa.uchiyama@ompu.ac.jp

PURPOSE

Many drug candidates have low solubility. Hence, improving solubility is still a challenging task in drug development. The amorphous state shows a high dissolution property compared to the crystalline state (1). Amorphous formulation of drugs alone poses challenges due to recrystallization during the dissolution process and storage, and limited dissolution caused by low glass transition temperatures. Therefore, hydrophilic polymers are often used as a dispersing agent to enhance the physicochemical stability of amorphs state. Wax-based formulation, prepared with oil and fat with a solid form at 37ºC, is used for sustained drug release(2). In this study, wax-based formulation was investigated as a dispersing agent of amorphous drug. It was considered whether the dispersion of amorphous drug particles to fat enables improved dissolution and permeation properties.

OBJECTIVE(S)

- Preparation of Wax-based formulation containing amorphous powders.
- Improvement of solubility and permeability of carvedilol as a poorly-water soluble drug.

METHOD(S)

Carvedilol was used as a model drug with low solubility. The chemical structure of carvedilol is shown in Figure 1. Amorphous carvedilol was prepared using the melt-quenching method, using a hot plate with a magnetic stirrer and liquid nitrogen. A stainless-steel cup was filled with carvedilol powder. A hot plate was used to heat the cup containing the sample for 5 minutes at 150ºC. Furthermore, the cup containing the melted sample was submerged in liquid nitrogen for 30 seconds without exposing the melted samples. Quenched sample was removed from the stainless-steel cup and crushed with a pestle and mortar. Then their samples was sieved with 150 mesh sieve. The crystallinity was determined using an X-ray diffractometer. The glass transition temperature was evaluated by differential scanning calorimetry. A solubility test of the powder sample was performed using a pH 6.8 phosphate buffer solution in a shaking bath at 37ºC. The wax-based formulation was prepared by dispersing amorphous carvedilol to glyceryl distearate for 10 min at 37ºC. The dissolution and permeability of carvedilol from wax-based formulation was evaluated by the μFlux™ system (Pion Inc.).

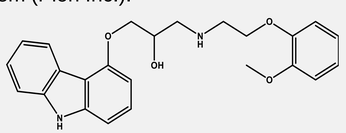

Figure 1 The Chemical structure of carvedilol.

RESULT(S)

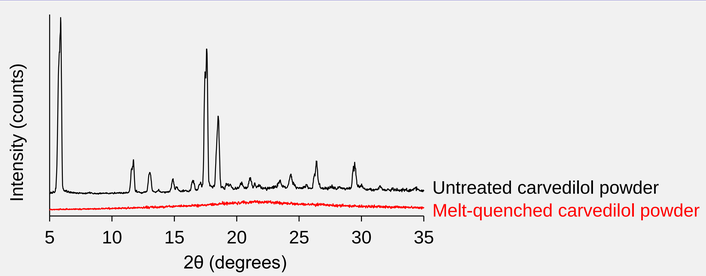

Figure 2 Powder X-ray diffraction (PXRD) patterns of untreated and melt-quenched carvedilol powders.

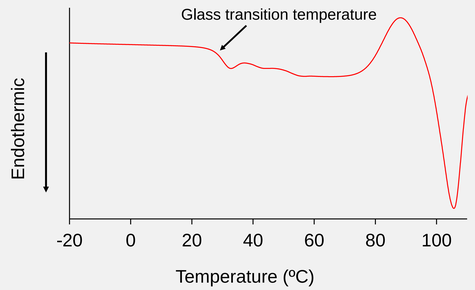

Figure 3 Differential scanning calorimetry (DSC) thermograms of Melt-quenched carvedilol powder

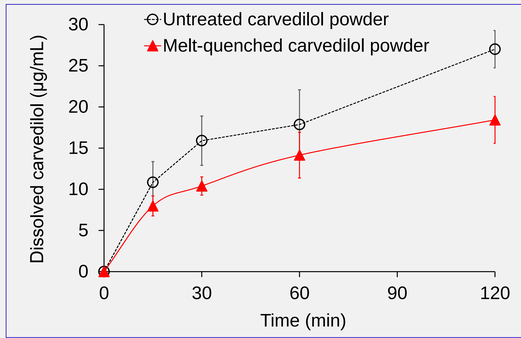

Figure 4 Dissolution profiles of untreated and melt-quenched carvedilol powders in pH 6.8 phosphate buffer solution in a shaking bath at 37ºC.

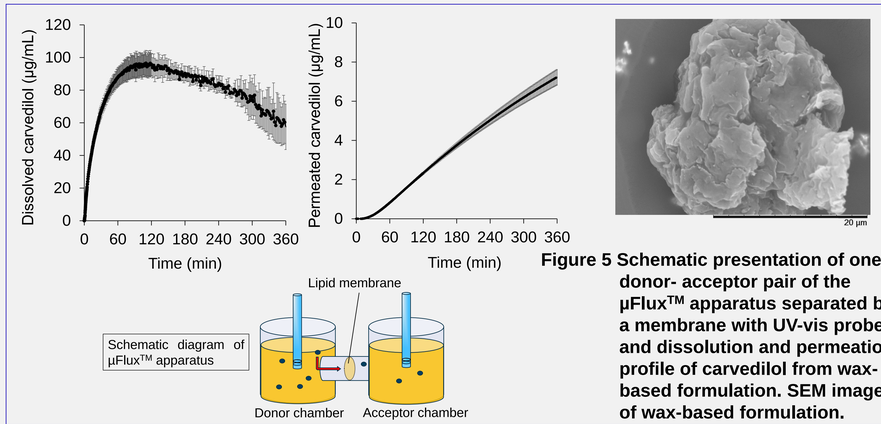

Figure 5 Schematic presentation of one donor- acceptor pair of the μFlux™ apparatus separated by a membrane with UV-vis probes and dissolution and permeation profile of carvedilol from wax-based formulation. SEM images of wax-based formulation.

CONCLUSION(S)

Figure 2 and Figure 3 (PXED and DSC)

The melt-quenched carvedilol powder showed an amorphous state in PXRD patterns. Its glass transition temperature was ca. 27ºC.

Figure 4 (Dissolution profiles)

The melt-quenched carvedilol showed low solubility/dissolution properties to untreated carvedilol. It was thought that carvedilol, with low glass transition temperature, became oily on contact with the test solution, resulting in limited dissolution from powder.

Figure 5 (Dissolution and permeation)

The dissolution property of carvedilol was improved by the wax-based formulation compared to powder formulation. In the permeation process, sustained and constant membrane permeation of carvedilol was observed. The wax-based formulation enables a sustained drug release, thereafter the released drug proceeds to the membrane permeation process.

FUNDING / GRANTS / ENCORE / REFERENCE OR OTHER USE

Reference

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