Novel pharmaceutical cocrystal consisting of paracetamol and trimethylglycine, a new promising cocrystal former

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Paracetamol (APAP), a frequently used antipyretic drug, has poor compression moldability. Recently, Karki *et al.* has reported a cocrystal of APAP and oxalic acid (OXA) to improve the disadvantage of crystalline powder APAP during production tableting[1)]. Although OXA is a widely-used salt-former, oxalates are a matter of contention due to their tendency to irritate biological tissues, their toxicity, and handling difficulties during the developmental stage[2, 3)]. Therefore, we conducted an exploratory screening assay to find a novel cocrystal former (coformer) for replacing OXA. Pharmaceutical ingredients approved for use in drugs, and coformers previously reported in the literature, were investigated as APAP coformers in total number of 70. As a result, we identified several novel cocrystals consisting of APAP and pharmaceutically acceptable ingredients, in particular combination with trimethylglycine (TMG) exhibited improved tabletability. The cocrystal (APAP-TMG at a molar ratio of 1:1) was characterized by X-ray diffraction analysis, infrared spectroscopy, and thermal analysis including thermogravimetry. The crystal structure of APAP-TMG revealed that it seemed to be classified as cocrystal, since no proton was transferred between the APAP and TMG molecules. The compression property and dissolution behavior of APAP-TMG were similar to those of the APAP-OXA cocrystal. In addition, taste sensing measurements suggested that TMG has a sweet and umami taste. Thus, TMG might suppress the bitterness of APAP, since TMG has been used as sweetening ingredient in food industry. From these results, TMG could be a safe and promising pharmaceutical coformer that could replace OXA and/or other coformers which can irritate tissues.

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