Stabilization and gelation mechanism of clarithromycin tablets under low pH conditions

Sadahiro Fujiki

Department of Pharmaceutical Engineering and Drug Delivery Science,

Graduate School of Pharmaceutical Sciences

It has been reported that tablets of 6-O-methylerythromycin (clarithromycin; CAM), a 14-membered macrolide antibiotic, are especially stable under low pH conditions such as in gastric fluid, and showed excellent antibacterial efficiency even though CAM molecules themselves are rapidly decomposed Therefore, the purpose of the present study is to clarify the stabilization mechanism of CAM tablets under low pH conditions.

From the results of stability and dissolution tests, the optimal decomposition rate constant (K_{dec}) and dissolution rate constant (K_{dis}) at various pH values were calculated by curve-fitting to consecutive reactions. Consequently, $\log(K_{dec})$ increased as pH decreased. On the other hand, $\log(K_{dis})$ increased as pH decreased from 3.0 to 1.5, but decreased as pH decreased from 1.5 to 1.0. The disintegration time of commercially available tablets at pH 1.0 and 1.2 was found to be delayed, resulting in a decrease of K_{dis}. In addition, the formation of a transparent gel on the surface of tablets, which were withdrawn from the disintegration apparatus just after 30 min at pH 1.0, was also observed. Furthermore, from powder X-ray diffraction, HPLC and elemental analysis, the delay in disintegration time might be attributable to the formation of a transparent gel, formed by the reaction between CAM molecule and hydrochloric acid under low pH conditions, on the surface of CAM tablet.

In conclusion, we demonstrated for the first time that CAM tablets form a gel structure on their surface under low pH conditions. The gel structure is considered to prevent gastric fluid from penetrating the tablet, resulting in reduced decomposition of CAM following oral administration, with the same effect as an enteric coating. Moreover, CAM tablets may be stable under low-pH gastric conditions, even if the CAM molecule itself is susceptible to rapid decomposition, and show excellent efficacy toward infective diseases.