

日本薬局方無菌試験法に収載された培地の微生物検出能に関する研究*³

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Study on Microbial Detectability with the Mandated Media for the Sterility Test in the Japanese Pharmacopoeia*³

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Summary

The Japanese Pharmacopoeia (JP) 4.06 Sterility Test mandates that pharmaceuticals are tested by culturing for not less than 14 days in both fluid thioglycollate medium (FTM) and soya-bean casein digest medium (SCDM). In this study, we verified the suitability of FTM and SCDM for detecting a total of 8 bacterial strains, consisting of five species (*Bacillus subtilis*, *Candida albicans*, *Clostridium sporogenes*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*) designated in the Sterility Test and three species (*Methylobacterium extorquens*, *Mycobacterium chelonae*, and *Serratia marcescens* subsp. *marcescens*) which were detected as contaminants in recalled pharmaceuticals. When FTM and SCDM were inoculated with the microbial species described in the Sterility Test at not more than 100 colony-forming units (CFU) according to the Growth Promotion Test in the JP 4.06 Sterility Test, microbial growth was detected in all combinations of the microbial species and media examined. However, at the 1 log₁₀ CFU inoculation level, which is similar to the low bacterial level required by the United States Pharmacopoeia (USP), microbial growth was observed for *B. subtilis* and *C. albicans* in SCDM and for *C. sporogenes* in FTM, but not for *P. aeruginosa* or *S. aureus* in FTM. Based on these findings, it is considered that FTM affords relatively low microbial detectability, and other media with higher detectability should be considered. Furthermore, among the bacteria found as contaminants in recalled pharmaceuticals, *M. extorquens* was not detected after 28 days of incubation in FTM, even when inoculated at the 3 log₁₀ CFU level. In contrast, when *M. extorquens* was inoculated into SCDM at the 2 log₁₀ CFU level required by the JP 4.06 Sterility Test, the detection rate was around 44.4% at 14 days of incubation, reaching 100% at 28 days. Therefore, it is considered crucial to conduct incubation for 14 days or more, as indicated by the JP 4.06 Sterility Test.

Key words

Japanese Pharmacopoeia, Sterility Test, Fluid thioglycollate medium, Soya-bean casein digest medium