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Ultra-high performance liquid chromatography tandem mass spectrometry for the determination of five glycopeptide antibiotics in food and biological samples using solid-phase extraction☆

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ABSTRACT

This paper demonstrated the development and validation of an ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC–MS/MS) method for simultaneous determination of five glycopeptide antibiotics in food and biological samples. The target glycopeptide antibiotics were isolated from the samples by solvent extraction, and the extracts were cleaned with a tandem solid-phase extraction step using mixed strong cation exchange and hydrophilic/lipophilic balance cartridges. Subsequently, the analytes were eluted with different solvents, and then quantified by UHPLC–MS/MS in the positive ionization mode with multiple reaction monitoring. Under optimal conditions, good linear correlations were obtained for the five glycopeptide antibiotics in the concentration range of 1.0 μg/L to 20.0 μg/L, and with linear correlation coefficients >0.998. Employing this method, the target glycopeptide antibiotics in food and biological samples were identified with a recovery of 83.0–102%, and a low quantitation limit of 1.0 μg/kg in food and 2.0 μg/L in biological samples with low matrix effects.

1. Introduction

Antibiotics are a type of antimicrobial drug that have been used for more than 80 years to fight illnesses, and have greatly reduced death from serious infectious diseases [1]. Unfortunately, these drugs have been so widely used that they have helped create bacteria that are outliving the drugs used to treat them. Antibiotic resistance is the ability of microbes to resist the effects of drugs. Resistant bacteria can multiply and spread easily and quickly, causing severe infections and posing a serious risk to human health [2–4]. Glycopeptide antibiotics are composed of glycosylated cyclic or polycyclic nonribosomal peptides that inhibit the late stages of bacterial cell wall peptidoglycan synthesis [5,6]. They are effective at low concentrations against the majority of Gram-positive bacteria, and are particularly useful in the treatment of methicillin-resistant staphylococcus aureus and methicillin-resistant staphycoccus epidermidis [7].

Avoiding clinical abuse and passive exposure are key ways to prevent the creation and spread of antibiotic resistance. People are mainly exposed to antibiotics and their residues from drinking water and food, which has been confirmed by biomonitoring-based studies [8–11]. Because excessive antibiotic residues have undesirable effects on consumer health, including the development of allergic reactions and resistant bacteria, there is an urgent need for sensitive and reliable analytical methods to monitor the concentrations of antibiotics residues in food, environment, and biological samples [12,13]. Currently, different analytical methods have been established for the determination of glycopeptide antibiotics. Yu et al. [14] described a direct fluorescence polarization assay for the detection of vancomycin, teicoplanin, and telavancin in biological samples [14]. In addition, high-performance liquid chromatography coupled with an ultraviolet detector has also been used for the determination of vancomycin and teicoplanin in serum and urine samples [15]. High performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS) can provide detailed molecular information and has already gained popularity as an analytical platform for the screening of antibiotics [16,17]. For example, Tsai et al. described the simultaneous determination of eight glycopeptide

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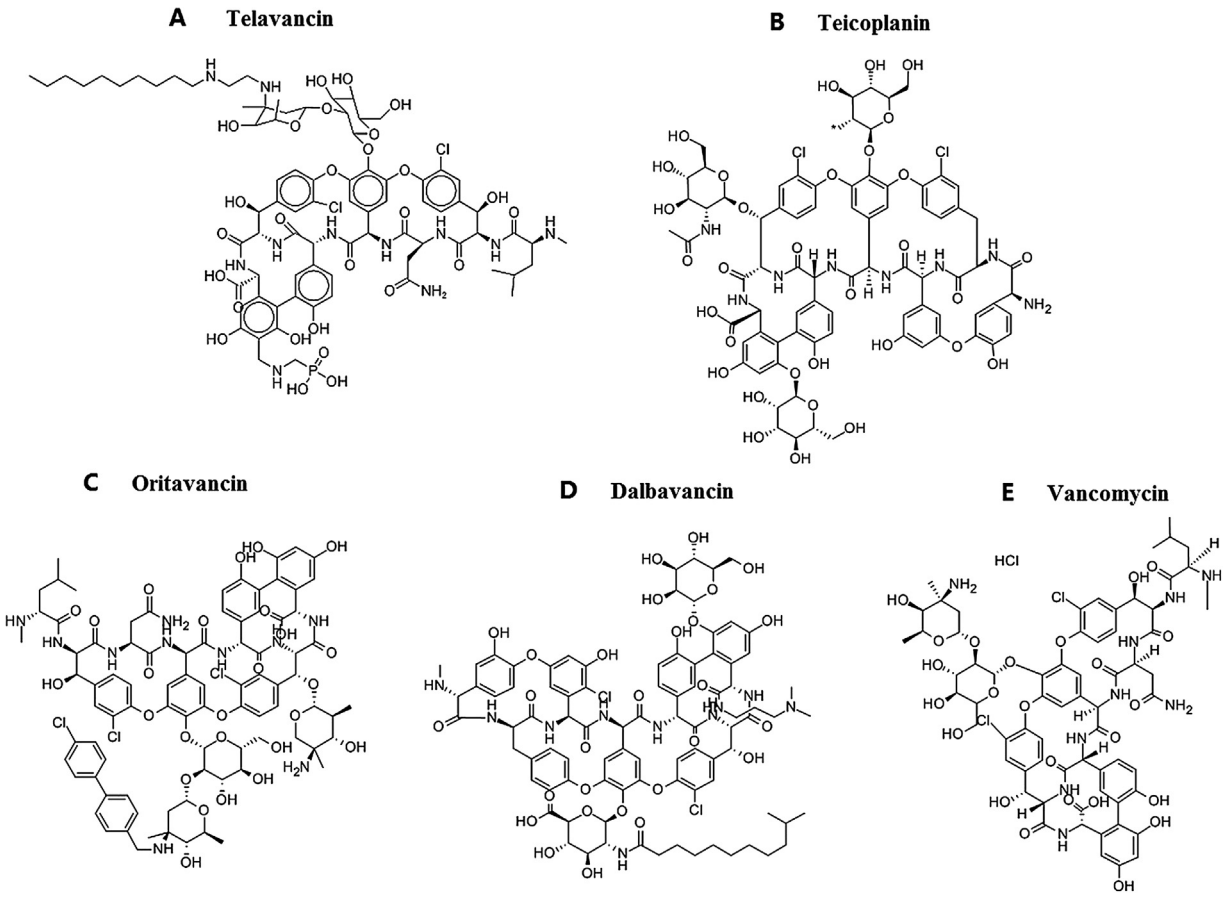

Fig. 1. Chemical structures of the most commonly glycopeptide antibiotics.

and lipopeptide antibiotics in biological samples [18]. Kim and co-workers used a direct injection-based simple, accurate, and robust HPLC-MS/MS method to determine teicoplanin in human plasma [19]. Wang et al. used solid-phase extraction (SPE) and HPLC-MS to quantitatively determine telavancin in pregnant baboon plasma [20].

Despite the rapid development of advanced instruments for the analysis of antibiotics, highly efficient sample preparation is still particularly important for complex samples and trace-level analysis. Food and biological samples are complex sample matrix that mainly contains proteins and fat, which often interfere with analytical procedures [21,22]. Therefore, the extraction and clean up of target antibiotics from the matrix is one of the most difficult steps in the analysis of antibiotics. The most commonly used techniques for the isolation of antibiotics from milk include liquid–liquid extraction [23–25] and SPE [26–30]. SPE has gained increasing popularity due to its ease of operation, complete phase separation, and the fact that disposal of large quantities of organic solvents is avoided [31]. However, choosing the appropriate SPE method for each application is vital. Hydrophilic–lipophilic balance (HLB) columns containing divinylbenzene and N-vinyl-pyrrolidone groups have been widely used in many cases. However, due to the absence of chargeable functional groups and negligible silanol activities, they are less effective with either positively and negatively charged molecules [32]. For the purpose of mitigating the strong interference of matrices, a tandem SPE method has frequently been employed for the clean-up of complicated matrices. You and Lydy established a tandem SPE clean-up method for the simultaneous analysis of pyrethroid, organophosphate, and organochlorine pesticides in fish tissue [33]. Renew and co-workers reported a tandem SPE technique for the clean-up of nine antibiotics in wastewater [34].

In this work, we demonstrated the feasibility of using ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC–MS/MS) coupled with tandem SPE for the quantitative determination of glycopeptide antibiotics including telavancin, teicoplanin, oritavancin, dalbavancin, and vancomycin. Fig. 1 shows the chemical structures of the selected glycopeptide antibiotics. The linearity of the calibration curve, recovery, and limits of detection were assessed to ensure the applicability of the developed method. This method was successfully used to determine the concentrations of the aforementioned antibiotics in food and biological samples.

2. Experimental section

2.1. Chemicals and instrumentation

Vancomycin, telavancin, oritavancin, dalbavancin, and teicoplanin were purchased from Guangzhou Anrun Chemical Reagent Company Ltd. (Guangzhou, China). Formic acid, methanol, and acetonitrile were purchased from Merck (Germany). Ultrapure water was from a laboratory water purification system (Sartorius, Germany) and used throughout the study. C18 cartridges, hydrophilic-lipophilic balance (HLB), and weak cation exchange (WCX), weak anion exchange (WAX), mixed strong cation exchange (MCX), and mixed strong anion exchange (MAX) SPE columns were purchased from Waters Corporation (Milford, MA, USA). The chro-