Characterization and classification of adverse drug interactions

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Combined use of multiple drugs may cause adverse events. Drug interactions can lead to an increase or a decrease of drug effects or other serious reactions. For example, coadministration of a drug metabolized by Cytochrome P450 3A4 (CYP3A4) and a drug inhibiting CYP3A4 results in delayed clearance and elevated blood levels of the former drug, which increases and prolongs both its therapeutic and adverse effects. Known information about potential risks of drug interactions is described in drug package inserts. The package inserts information for Japanese marketed drugs is provided by the JAPIC (Japan Pharmaceutical Information Center) database, which is integrated in the GenomeNet pharmaceutical products database, together with the KEGG DRUG database. Drugs or drug classes which cause adverse interactions are listed in each JAPIC entry. In the previous work, we extracted interaction data from the drug package inserts and created drug-drug interaction network. We regarded the JAPIC entries that have the same compound for their therapeutic effect as the same drug by using the KEGG DRUG IDs (D numbers). In this study, we merged D numbers into the drug groups using the Anatomical Therapeutic Chemical (ATC) classification and explored the relationship between drug interaction mechanisms and interaction characteristics. The interaction characteristics include drug properties such as targets, metabolizing enzymes, pharmaceutical effects and drug categories, and were examined at each ATC classification level.