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Autores	Silveira, Anne Michelli Reis ; Duarte, Gustavo Henrique Bueno ; Fernandes, Anna Maria Alves De Piloto ; Garcia, Pedro Henrique Dias ; Vieira, Nelson Rogerio ; Antonio, Marcia Aparecida ; Carvalho, Patricia De Oliveira
Autor (es) USF	Silveira, Anne Michelli Reis ; Duarte, Gustavo Henrique Bueno ; Fernandes, Anna Maria Alves De Piloto ; Garcia, Pedro Henrique Dias ; Vieira, Nelson Rogerio ; Antonio, Marcia Aparecida ; Carvalho, Patricia De Oliveira
Autores Internacionais	
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Resumo	Rosuvastatin is a well-known lipid-lowering agent generally used for hypercholesterolemia treatment and coronary artery disease prevention. There is a substantial inter-individual variability in the absorption of statins usually caused by genetic polymorphisms leading to a variation in the corresponding pharmacokinetic parameters, which may affect drug therapy safety and efficacy. Therefore, the investigation of metabolic markers associated with rosuvastatin inter-individual variability is exceedingly relevant for drug therapy optimization and minimizing side effects. This work describes the application of pharmacometabolomic strategies using liquid chromatography coupled to mass spectrometry to investigate endogenous plasma metabolites capable of predicting pharmacokinetic parameters in predose samples. First, a targeted method for the determination of plasma concentration levels of rosuvastatin was validated and applied to obtain the pharmacokinetic parameters from 40 enrolled individuals; then, predose samples were analyzed using a metabolomic approach to search for associations between endogenous metabolites and the corresponding pharmacokinetic parameters. Data processing using machine learning revealed some candidates including sterols and bile acids, carboxylated metabolites, and lipids, suggesting the approach herein described as promising for personalized drug therapy.
Fomento	