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Data in Brief

Toxicogenomic analysis of pharmacological active coumarins isolated from *Calophyllum brasiliense*

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ABSTRACT

Calophyllum brasiliense (Calophyllaceae) is a tropical rain forest tree, mainly distributed in South and Central America. It is an important source of bioactive natural products like, for instance soulatrolide, and mammea type coumarins. Soulatrolide is a tetracyclic dipyranocoumarins and a potent inhibitor of HIV-1 reverse transcriptase and *Mycobacterium tuberculosis*. Mammea A/BA and A/BB coumarins, pure or as a mixture, are highly active against several leukemia cell lines, *Trypanosoma cruzi* and *Leishmania amazonensis*. In the present work, a toxicogenomic analysis of Soulatrolide and Mammea A/BA + A/BB (3:1) mixture was performed in order to validate the toxicological potential of this type of compounds. Soulatrolide or mixture of mammea A/BA + A/BB (3:1) was administered orally to male mice (CD-1) at dose of 100 mg/kg/daily, for 1 week. After this time, mice were sacrificed, and RNA extracted from the liver of treated animals. Transcriptomic analysis was performed using Affymetrix Mouse Gene 1.0 ST Array. Robust microarray analysis (RMA) and two way ANOVA test revealed for mammea mixture treatment 46 genes upregulated and 72 downregulated genes; meanwhile, for soulatrolide 665 were upregulated and 1077 downregulated genes. Enrichment analysis for such genes revealed that in both type of treatments genetic expression were mainly involved in drug metabolism. Overall results indicate a safety profile. The microarray data complies with MIAME guidelines and are deposited in GEO under accession number GSE72755.

Specifications	
Subject area	Chemistry
More specific subject area	Natural Products–Toxicogenomics
Organism/cell line/tissue	CD-1 mice
Sex	Male
Sequencer or array type	Affymetrix mouse gene chip 1.0 Array
Data format	Raw and Analyzed with RMA and two way ANOVA
Experimental factors	Comparison of control (SSI) and treatment (100 mg/Kg) with soulatrolide or mammea A/BA + A/BB (3:1) mixture
Experimental features	RNA was extracted from the liver of mice after 1 week of treatment, converted to cDNA and hybridized to Affymetrix arrays
Consent	All animal work was conducted in strict accordance with relevant national and international guidelines. The study protocol IG-2005-13 was approved by the Animal and Ethics Experiment Board of School of Medicine of Universidad Nacional Autónoma de México
Sample source location	Facultad de Medicina, Universidad Nacional Autónoma de Mexico, Mexico City, Mexico.

1. Direct link to deposited data

The data is deposited in GEO under accession number GSE72755: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE72755.

2. Value of the data

- The data provide a toxicogenomics signature of two types of pharmacological active coumarins that could be for comparison in other studies of this kind.

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Table 1
Analysis of pathways enriched by coumarins treatments (Soulatrolide 1744 DEG's and Mammea A/BA + A/BB-120 DEG's).

Treatment/genes	Pathway	P-Value	Count
Mammea A/BA + A/BB (3:1)	KEGG_PATHWAY:	4.96E-5	8
Down Regulated Genes	00830 Retinol metabolism		
(Fold Change >1.5 < −1.5; p-value <0.05).	KEGG_PATHWAY:	0.00103	5
	00982		
	Drug metabolism		
Mammea A/BA + A/BB (3:1)	KEGG_PATHWAY	0.005272	4
Up regulated genes	04060:Cytokine–cytokine		
(fold change >1.5 < −1.5; P-VALUE <0.05).	receptor interaction		
Soulatrolide	KEGG_PATHWAY	3.36E-11	34
Down regulated genes	00980:Metabolism of xenobiotics by cytochrome P450		
(fold change >1.5 < −1.5; p-value <0.05).	KEGG_PATHWAY	4.94E-10	38
	00982:Drug metabolism		
	KEGG_PATHWAY	2.36E-8	52
	00830:Retinol metabolism		
Soulatrolide	KEGG_PATHWAY	3.359E-11	34
Up regulated genes	00980:Metabolism of		
(Fold change >1.5 < −1.5; p-value <0.05).	xenobiotics by CYP		
	P450		
	KEGG_PATHWAY	4.94E-10	38
	00982:Drug		
	metabolism		
	KEGG_PATHWAY	2.36E-8	52
	00830:Retinol		
	metabolism		

- The data provide an insight in the metabolism induced by pharmacological active coumarins.
- This data provides the first toxicogenomic analysis on mammea type coumarins particularly mammea A/BA and A/BB, and on tetracyclic coumarins such as soulatrolide.

3. Experimental design, materials and methods

3.1. Toxicogenomics assay

A total of 12 male mice (*Mus musculus*) strain CD1 (Charles River), body weight 25 ± 4 g, with an age of two month old, were provided by the School of Medicine of the National University of Mexico (UNAM). The animals were kept under standard conditions in ventilated boxes (12 h light/dark and 27 ± 2 °C) and fed with RatChow™ divided in three groups depending on treatments: 1)Soulatrolide, 2)Mammea (A/BA + A/BB 3:1) and 3) Isotonic Saline Solution 0.9% (control). Treatments were administered orally for 7 days at a dose of 100 mg/Kg/daily [1]. All animal work was conducted in strict accordance with relevant national and international guidelines. The study protocol IG-2005-13 was approved by the Animal and Ethics Experiment Board of School of Medicine of Universidad Nacional Autónoma de México. Liver of animals was immediately obtained after sacrificed and samples immediately homogenized with PureLink® RNA Mini Kit.The amount of RNA was determined by using Nanodrop®2000 (ThermoScientific, Waltham, MA, USA), integrity of RNA was determined using a Bioanalyzer®(Agilent, Waldbronn, Germany) cDNA synthesis, target hybridization, probe array washing, staining and subsequent probe array scanning were done according to the standard protocol 3′IVT Express Kit User Manual (Affymetrix). Microarray analysis was performed by using Affymetrix Mouse Gene Chip 1.0 Array, using three microarrays per treatment.

3.2. Microarray experiments and data acquisition processing

Signal intensities from each array were analyzed using Partek Genomic Suite 6.4 (Partek Inc., Missouri, USA). Raw intensity probe values were normalized using robust multiarray analysis background correction (RMA). A two way ANOVA was performed to identify differentially expressed genes. Only genes with statistically significant differences in expression levels (p-value < 0.05) and a fold change criteria of ≥1.5and ≤− 1.5 were included in the final set of differentially expressed genes (Table 1).

3.3. Gene ontology (GO) analysis

The list of genes with significantly changed expression levels for both treatments revealed 46 genes up and 72 downregulated genes; meanwhile, for soulatrolide 665 up and 1077 downregulated genes were used as input lists for the DAVID Functional Annotation Clustering tool [2]. This open source software provides an enrichment analysis of annotation and gene ontology terms based on a GO: TermFinder. The corrected p-value was obtained by applying Bonferroni correction [2].

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