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ORIGINAL ARTICLE

Basic Study

Metabolomic profiling for identification of metabolites and relevant pathways for taurine in hepatic stellate cells

Xin Deng, Xing-Qiu Liang, Fei-Guo Lu, Xiao-Fang Zhao, Lei Fu, Jian Liang

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Author contributions: Deng X performed the majority of experiments and analyzed the data; Liang XQ wrote the paper; Lu FG, Zhao XF and Fu L participated equally in the culture and treatment of hepatic stellate cells; Liang J designed and coordinated the research.

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Abstract

AIM

To develop a reliable and simple method to identify important biological metabolites and relevant pathways for taurine in hepatic stellate cells (HSCs), in order to provide more data for taurine therapy.

METHODS

All the biological samples were analyzed by using high-performance liquid chromatography-time electrospray ionization/quadrupole-time of flight mass spectrometry. Principal component analysis and partial least squares discriminant analysis were used to identify statistically different metabolites for taurine in HSCs, and metabolomic pathway analysis was used to do pathway analysis for taurine in HSCs. The chemical structure of the related metabolites and pathways was identified by comparing the m/z ratio and ion mode with the data obtained from free online databases.

RESULTS

A total of 32 significant differential endogenous metabolites were identified, which may be related to the mechanism of action of taurine in HSCs. Among the seven relevant pathways identified, sphingolipid metabolism pathway, glutathione metabolism pathway and thiamine metabolism pathway were found to be

the most important metabolic pathways for taurine in HSCs.

CONCLUSION

This study showed that there were distinct changes in biological metabolites of taurine in HSCs and three differential metabolic pathways including sphingolipid pathway, glutathione pathway and thiamine metabolism pathway might be of key importance in mediating the mechanism of action of taurine in HSCs.

Key words: Natural taurine; Hepatic stellate cells; Pathway; High performance liquid chromatography-time electrospray ionization/quadrupole-time of flight mass spectrometry; Metabolomics

Core tip: At the cellular level, it is reported that the activation of hepatic stellate cells (HSCs) in the subendothelial space may result in hepatic fibrosis. Although taurine was found to increase HSC apoptosis significantly, its molecular mechanisms are still unknown. This study developed a reliable and simple method to identify important biological metabolites and relevant pathways for taurine in HSCs, in order to provide more data for taurine therapy. We found that there were distinct changes in the biological metabolites of taurine in HSCs, and identified three differential metabolic pathways that might be of key importance in mediating the mechanism of action of taurine in HSCs.

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INTRODUCTION

Hepatic fibrosis (HF) is a scarring process in which the liver forms scar tissue due to an abnormal deposition of extracellular matrix (ECM)[1]. Recently, more and more attention has been paid to the molecular mechanisms of hepatic fibrosis. At the cellular level, it is reported that the activation of hepatic stellate cells (HSCs) in the subendothelial space may result in hepatic fibrosis[2]. Moreover, reversal or apoptosis of activated HSCs has been proven to be beneficial for the treatment or regression of hepatic fibrosis[3].

Metabolomics methods can be used to characterize the metabolic profiles of a biological system. As metabolites with relatively low molecular weight are downstream products of biological processes, their identity and concentrations in a living biological system can provide biochemical signatures for globally tracking the physiological effects and exploring the drug effects[4-6]. A previous study[7] systematically analyzed the protective effects of traditional Chinese medicine Hongshan Capsules, and identified the potential target biomarkers through the metabonomic approach of ultra-performance liquid chromatography coupled to mass spectrometry. Therefore, metabolomics methods can be used to identify biomarkers for clinical drug therapy, especially in cancer research[8,9].

Taurine, a beta-amino acid with a simple structure that is extracted from animal tissue, has been investigated as a promising drug for the treatment of many hepatic injuries[10-13]. In previous studies, taurine was showed to significantly increase the apoptosis of HSCs and raise the levels of 19 proteins related to cellular apoptosis or oxidation in HSCs[14,15]. However, the exact metabolic pathways and molecules involved in the mechanisms of action of taurine are still unknown. Therefore, this study aimed at developing a reliable and simple method to find important biological metabolites and pathways that are related to taurine in HSCs, in order to provide more data for taurine therapy.

MATERIALS AND METHODS

Cell culture and cell viability assay

Human HSCs (LX-2) were obtained from Xiangya Central Experiment Laboratory of Central South University (Changsha, China) and were incubated in DMEM (Thermo Scientific Hyclone, Logan, UT, United States) containing 100 U/mL penicillin (North China Pharmaceutical, China), 100 μg/mL streptomycin (North China Pharmaceutical, China) and 10% fetal bovine serum (Biochrom AG, Berlin, Germany) at room temperature in an incubator with 50 mL/L CO_2 and saturated humidity. The culture medium was replaced every two days. Trypsin (0.25%) was added for digestion when the confluence of HSCs reached 80%-90% and the supernatant was discarded after centrifugation at 1000 r/min for 5 min. Then, the cells were resuspended to a density of 5×10^5/mL.

MTT method was used to determine the optimum drug concentration of taurine for the subsequent study. Briefly, HSCs were added into a 96-well plate at a density of 5×10^4 cells per well. Natural taurine (Yuanlong Pearl Co. Ltd., Beihai, China) was dissolved in dimethyl sulphoxide (DMSO) at a concentration of 8 mol/L, and then diluted with 2% DMEM to 10, 20, 40, 60, 80 and 100 mmol/L. Six replicates were applied for each concentration of taurine and the whole reaction system was maintained for 48 h. Cells treated with DMSO alone were used as controls. Subsequently, 10 μL of MTT solution (5 mg/mL in PBS) was added and the cells were further incubated for 4 h at 37 ℃. Then, the reaction was terminated by the addition of 100 μL DMSO and absorbance was measured at 495 nm using

Table 1 Gradient elution program of the mobile phase

Time (min)	Flow rate (mL/min)	Solution B (%)
0	0.35	5
1	0.35	5
6	0.35	20
9	0.35	50
13	0.35	95
15	0.35	95

a microplate reader (Molecular Devices, United States). Based on the results, the concentration of 40 mmol/L was chosen as the optimum drug concentration of taurine for the following study.

Sample preparation

For the following metabolomic study, HSCs were incubated in 10-cm culture dishes until approximately 70% confluence and then treated with celastrol and other control drugs for 12 h. Each dish was washed twice at 37 ℃ with PBS after removing the culture medium, and dried in the vacuum. Then, the cells were quenched by adding 1.5 mL HPLC-grade methanol at -80 ℃ and were separated from the culture dish with a cell lifter (Fisher Scientific, United States). The cell solution was subsequently transferred to a 2 mL centrifuge tube and frozen in liquid nitrogen until liquid-liquid extraction. Six replicates were applied for 40 μmol/L of natural taurine for 48 h as the test group and the same concentration of DMSO was used as the control group. To avoid cell cytotoxicity, the final concentration of DMSO must be less than 0.1% for both the taurine group and the control group. Additionally, five parallel blank culture dishes were trypsinized and counted for the normalizing the subsequent analysis.

After incubation, the culture medium was removed generally and the residual medium was removed by using 2 mL 0.9% [w/v] ice-cold isotonic saline (NaCl) to arrest cellular metabolism. Subsequently, the cells were added with 1 mL cold methanol/water (4:1) to quench cells and then collected in 2 mL centrifuge tubes. Then, the cells were ultrasonicated for 5 min (5 s ultrasonication at a 10-s interval) in an ice bath and centrifuged at 13000 *g* for 10 min at 4 ℃. Finally, the supernatant was dried with nitrogen and stored at -80 ℃ before detection.

Chromatography and spectrometry conditions

Samples were resolved with acetonitrile/water (1:1, v/v) mixture according to the cell number counted in advance and detected by high performance liquid chromatography-electrosprayionization/quadrupole-time-of-flight mass spectrometry (HPLC ESI/Q-TOF MS) (Agilent Technologies, United States). All the samples were separated on an Agilent C18 column (2.1 mm × 100 mm, 1.8 μm, Agilent Technologies, United States) with the following parameters: injection volume, 4 μL; flow rate, 0.35 mL/min; column temperature, 40 ℃. The mobile phase was composed of (A) 0.1% formic acid water solution and (B) 0.1% formic acid acetonitrile solution. The gradient elution program (Table 1) was linearly increased from 5% to 20% B (0-6 min), stable at 50% B (6-8 min), linearly increased to 95% B (8-12 min) and maintained for 3 min. The quality control (QC) was prepared and injected before the injection of test samples.

Both ESI^+ and ESI^- ionization modes were used to find the potential specific metabolites of taurine in HSCs. The ionization mode was set at a capillary voltage of 4.0 kV (ESI^+) or 3.5 kV (ESI^-), cone voltage of 35V (ESI^+) and 50V (ESI^-), source temperature of 100 ℃, cone gas flow of 50 L/h, desolvation gas flow, desolvation gas flow of 600 L/h, and desolvation gas temperature of 350 ℃. Data were collected in the centroid mode with the mass range (m/z) of 50-1000, scan time of 0.03 s and inter-scan delay of 0.02 s. To lock the mass system, 100 pg/μL leucine-enkephalin (m/z 556.2771 in ESI^+ mode or m/z 554.2615 in ESI^- mode) at 0.05 mL/min with the frequency of 10 s was used.

Data processing and statistical analysis

After excluding the noise and background interference, raw mass spectral data of both ESI^+ and ESI^- modes were analyzed by using Mass Profiler (Agilent Technologies, United States) to generate data, including retention time, signal intensity and m/z ratio for peak identification. Subsequently, SIMCA-P 13.0 software (Umetric AB, CA, United States) was applied to do principal component analysis (PCA) to distinguish different scatters of the biological metabolites for taurine in HSCs, partial least squares discriminant analysis (PLS-DA) to find statistically different metabolites. Variable importance in the projection (VIP) plots (VIP > 1) of the PLS-DA was used to find the exact potential biomarkers. Finally, the structure of the related metabolites and pathways was identified by comparing the m/z ratio and ion mode with the data obtained from free online databases including Human Metabolome Database (HMDB) (www.hmdb.ca), Metlin metabolomics database (http://metlin.scripps.edu/) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway database (www.genome.jp/kegg/pathway.html). MetPA network software[16] (http://metpa.metabolomics.ca/Met PA/faces/Home.jsp) was used to do pathway analysis for taurine in HSCs.

RESULTS

Total ion current spectra of taurine in HSCs

In the current study, all the biological metabolites of taurine in HSCs were detected by HPLC-ESI/Q-TOFMS, which might provide useful information for unveiling the underlying molecular mechanisms of taurine in HSCs. The total ion current spectra of the samples

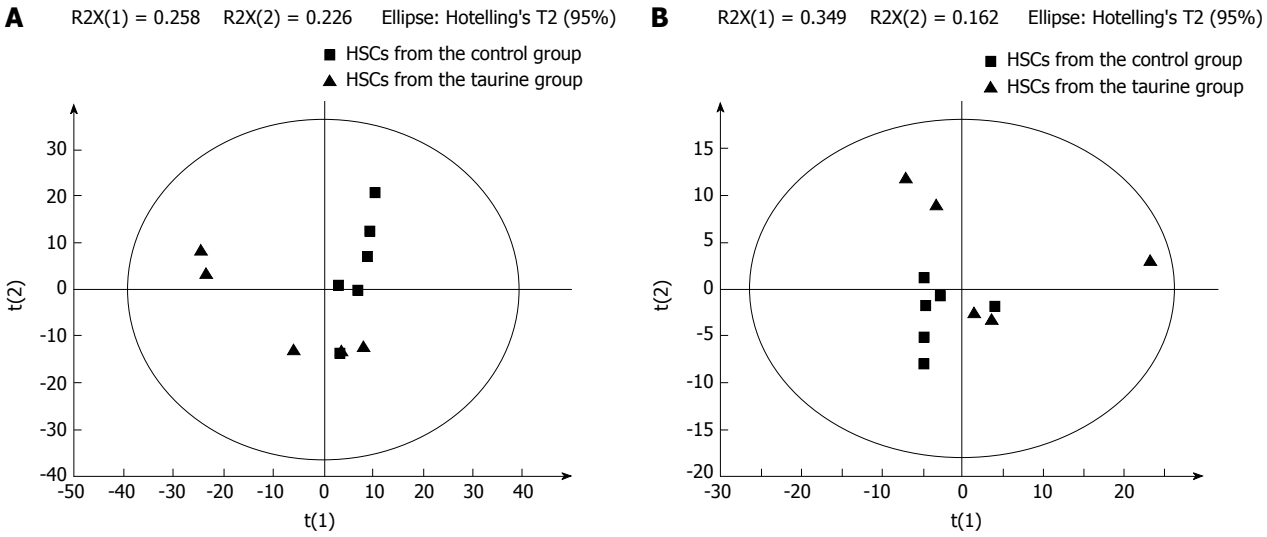

Figure 1 Principal component analysis plots of biological metabolites for taurine in hepatic stellate cells in electrosprayionization$^+$ mode (A) and in electrosprayionization$^-$ mode (B). HSCs: Hepatic stellate cells; ESI: Electrosprayionization.

between the control and taurine-treated HSCs differed greatly, suggesting that there might be some metabolic changes for taurine in HSCs.

PCA

PCA statistically divided all the detected metabolites into smaller clusters as principal components (PCs) to find the potential biomarkers. In this study, all the samples were classified into two small clusters between the control and taurine-treated cells in the PCA score plots (Figure 1), demonstrating that there were significant metabolic differences between the control and taurine-treated HSCs.

PLS-DA

Then, the potential important metabolites were further analyzed by using PLS-DA. Consistent with the results of PCA, PLS-DA plots showed two clear groups between the control and taurine-treated cells (Figure 2). Moreover, a total of 27 metabolites in ESI$^+$ mode and five metabolites in ESI$^-$ mode were found to be the significant metabolites between the control and taurine-treated cells (VIP > 1) (P < 0.05) (Table 2).

Structure identifications and pathway identification

The definite identity of the significant metabolites in the biological samples and their contributions to the biological processes are important for the current metabolomics study. Therefore, the structure of the related metabolites and pathways was identified by comparing the m/z ratio and ion mode with the data obtained from on-line free databases including HMDB (www.hmdb.ca), Metlin metabolomics database (http://metlin.scripps.edu/) and KEGG pathway database (www.genome.jp/kegg/pathway.html).

Additionally, 16 potential metabolic pathways were analyzed by MetPA network software and three significant metabolic pathways (sphingolipid metabolism, glutathione metabolism and thiamine metabolism) were found to be the most important metabolic pathways for taurine in HSCs (Table 3 and Figure 3).

DISCUSSION

In this study, a simple chromatography method coupled with pathway analysis by using high-performance liquid chromatography-time electrospray ionization/quadrupole-time of flight mass spectrometry (HPLC-ESI/Q-TOF-MS) was successfully performed for analyzing the mechanism of taurine in HSCs. A total of 32 significant differential endogenous metabolites were identified. Among the seven relevant pathways for taurine, sphingolipid metabolism pathway (Figure 4), glutathione metabolism pathway (Figure 5) and thiamine metabolism pathway were found to be the most important metabolic pathways for taurine in HSCs.

The sphingolipid metabolism pathway contributes greatly to structural functions and cellular signaling. For example, membrane sphingolipids can regulate cell proliferation, differentiation and death[17-19]. Increasing evidence shows that sphingolipids are important in stress and ligand-induced hepatocellular death, which can cause several liver diseases like steatohepatitis, ischaemia-reperfusion hepatic damage or hepatic cancer[20]. Additionally, increased levels of sphingolipids in specific cell subcompartments can cause liver dysfunctions and some inherited diseases. Tumour necrosis factor (TNF) is an important death receptor, and abnormal expression of TNF can cause many liver diseases[21]. Thus, TNF becomes an important target for liver disease. In this study, taurine was found to be able to regulate sphingolipid metabolism. Therefore, we hypothesize that taurine might be able to intervene the activation of HSCs and regulate TNF expression.

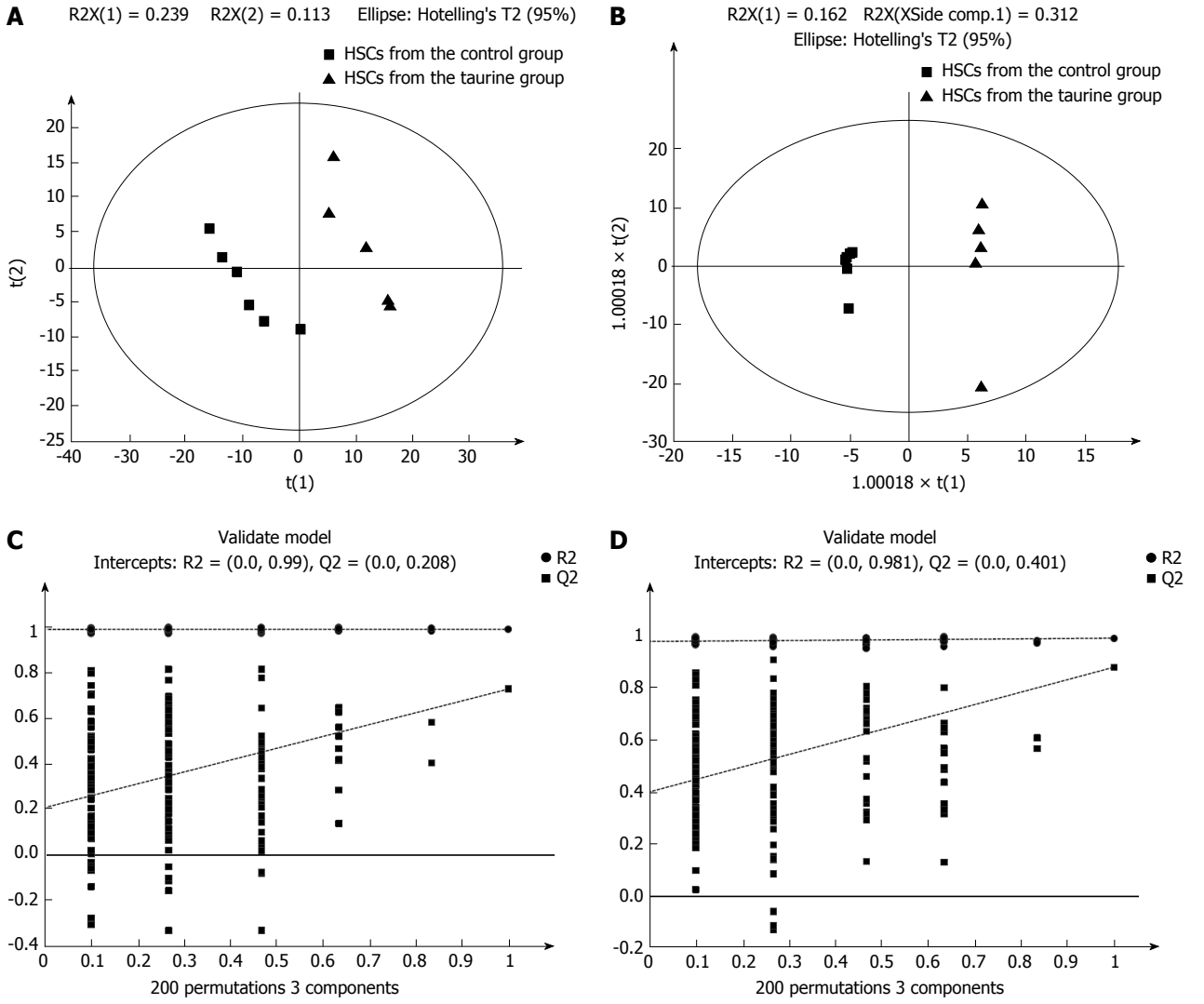

Figure 2 Partial least square discriminant analysis and validation of biological metabolites for taurine in hepatic stellate cells in electrosprayionization$^+$ mode and in electrosprayionization$^-$ mode. A: Partial least square discriminant analysis (PLS-DA) plots of biological metabolites for taurine in hepatic stellate cells (HSCs) in ESI$^+$ mode; B: PLS-DA plots of biological metabolites for taurine in HSCs in ESI$^-$ mode; C: Validation of biological metabolites for taurine in HSCs in ESI$^+$ mode; D: Validation of biological metabolites for taurine in HSCs in ESI$^-$ mode. ESI: Electrosprayionization; HSCs: Hepatic stellate cells.

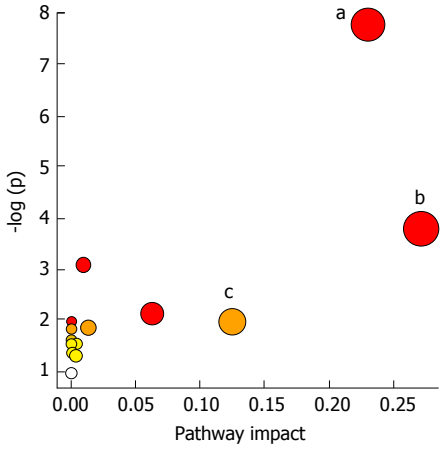

Figure 3 Potential pathways for taurine in hepatic stellate cells identified by using MetPA pathway analysis. [a]Sphingolipid metabolism pathway; [b]Glutathione metabolism pathway; [c]Thiamine metabolism pathway.

However, the exact mechanism of the action of taurine in the HSCs needs further investigation.

Besides, lysophosphatidylcholine (LysoPC) can affect HSCs through several mechanisms. First, LysoPC can inhibit proliferation of endothelial cells and increase their apoptosis, thereby affecting the molecular structure of the endothelium and the proliferation of vascular smooth muscle cells[22,23]. Second, LysoPC can downregulate endothelium-derived NO and activate the LOX-1 receptor to desensitize eNOS, thus causing endothelial dysfunction[24]. Furthermore, activation of HSCs can lead to increased expression of genes relevant to lipid accumulation and increased levels of intracellular lipids. In this study, LysoPC was found as the significantly different metabolite between the control and taurine-treated groups. LysoPC is an important plasma lipid cell signaling molecule for LDL oxidization and can be generated by phospholipase A2 hydrolysis or phosphatidylcholine (PC) oxidation[25]. Thus, we hypothesize that the interventional effect of taurine on HSCs is related with lipid metabolism. This

Table 2 Potential important biological metabolites in ESI$^+$ and ESI$^-$ modes for taurine in hepatic stellate cells

Number	Mode	VIP	RT (min)	m/z ratio	Compound name	Fold change (B/A)	*P* value
1	ESI$^+$	1.312	11.16	495.3338	PC (16:0)	-0.758↓	0.037
2	ESI$^+$	1.973	14.02	148.0160	2-oxo-4-methylthiobutanoic acid	-3.094↓	0.001
3	ESI$^+$	1.326	7.51	215.1890	Amino-dodecanoic acid	1.249↑	0.043
4	ESI$^+$	1.316	3.89	231.1475	Butyryl-L-carnitine	-1.711↓	0.041
5	ESI$^+$	1.644	8.87	273.2679	C16 Sphinganine	-0.837↓	0.034
6	ESI$^+$	1.329	0.74	161.1047	Carnitine	2.324↑	0.049
7	ESI$^+$	1.570	13.27	375.3125	Docosatetraenoyl Ethanolamide	2.200↑	0.017
8	ESI$^+$	1.706	11.46	399.3362	Palmitoylcarnitine	-1.419	0.005
9	ESI$^+$	1.484	11.01	199.1943	Dodecanamide	1.521↑	0.022
10	ESI$^+$	1.590	1.09	307.0848	Glutathione	-1.372↓	0.019
11	ESI$^+$	1.268	6.03	259.1792	Hexanoylcarnitine	-1.216↓	0.046
12	ESI$^+$	1.565	4.59	282.1684	Hydroxydesipramine	2.210↑↓	0.013
13	ESI$^+$	1.601	11.01	569.3486	LysoPC(22:5)	17.551↑	0.048
14	ESI$^+$	1.483	1.01	175.0482	N-acetylaspartate	-1.160↓	0.018
15	ESI$^+$	1.495	12.63	369.3254	N-palmitoyl isoleucine	1.375↑	0.017
16	ESI$^+$	1.557	12.15	369.3254	N-palmitoyl isoleucine	2.683↑	0.039
17	ESI$^+$	1.245	10.48	371.3045	N-stearoyl serine	-1.027↓	0.048
18	ESI$^+$	1.312	13.05	281.2728	Oleamide	-0.852↓	0.036
19	ESI$^+$	1.469	10.13	212.1417	Oxo-dodecenoic acid	1.750↑	0.019
20	ESI$^+$	1.595	11.24	479.3025	PC (15:1)/PE (18:1)	-1.141↓	0.018
21	ESI$^+$	1.284	11.30	521.3494	PC (18:1)	-0.727↓	0.048
22	ESI$^+$	2.021	8.93	317.2939	Phytosphingosine	-1.274↓	0.001
23	ESI$^+$	1.290	0.65	202.2163	Spermine	-0.874↓	0.039
24	ESI$^+$	1.443	9.90	301.2992	Sphinganine	-0.807↓	0.040
25	ESI$^+$	1.394	11.60	299.2835	Sphingosine	-0.949↓	0.026
26	ESI$^+$	1.430	12.34	427.3675	Stearoylcarnitine	-1.006↓	0.026
27	ESI$^+$	1.818	0.80	117.0791	Valine	-0.681↓	0.037
28	ESI$^-$	2.017	1.13	192.0270	Citric acid	-0.870↓	0.001
29	ESI$^-$	1.678	11.11	453.2859	Glycerophospho-N-Palmitoyl Ethanolamine	-1.125↓	0.011
30	ESI$^-$	2.076	11.46	479.3016	PC (15:1)	-1.697↓	0.000
31	ESI$^-$	1.648	0.69	264.1045	Thiamine	0.394↑	0.040
32	ESI$^-$	1.448	9.25	250.1204	Ubiquinone-1	1.538↑	0.031

Comparisons were done by two-sample *t*-test. A total of 27 metabolites in ESI$^+$ mode and 5 metabolites in ESI$^-$ mode were found to be the significant metabolites between the control and taurine-treated cells (VIP > 1) ($P < 0.05$). PC: Phosphatidylcholine; VIP: Variable importance in the projection; (↑): Up-regulated; (↓): Down-regulated.

Table 3 Results of MetPA pathway analysis

Pathway name	Compounds[1]	Expected[2]	Hits	Raw *P*[3]	FDR *P*[4]	Impact
Glutathione metabolism	38	0.23681	2	0.022	0.896	0.272
Sphingolipid metabolism	25	0.1558	3	0.000	0.033	0.231
Thiamine metabolism	24	0.14956	1	0.140	1	0.125
Citrate cycle (TCA cycle)	20	0.12464	1	0.118	1	0.063
Valine, leucine and isoleucine biosynthesis	27	0.16826	1	0.156	1	0.013
Cysteine and methionine metabolism	56	0.34898	2	0.046	1	0.009
Glyoxylate and dicarboxylate metabolism	50	0.31159	1	0.271	1	0.003
Glycerophospholipid metabolism	39	0.24304	1	0.218	1	0.003

[1]The total number of metabolites in each pathway; [2]The actually matched number according to the uploaded data; [3]The original *P*-value using enrichment analysis; [4]The adjusted *P*-value using false discovery rate. The table shows the detailed results from the pathway analysis. Since we tested many pathways at the same time, the *P*-values from enrichment analysis are further adjusted for multiple tests. In particular, the Hits is the actually matched number from the user uploaded data; the Raw *P* is the original *P*-value calculated from the enrichment analysis; the FDR *P* is the *P*-value adjusted using false discovery rate; the Impact is the pathway impact value calculated from pathway topology analysis. Sixteen potential metabolic pathways were analyzed by MetPA network software and three significant metabolic pathways (Sphingolipid metabolism, glutathione metabolism and thiamine metabolism) were found to be the most important metabolic pathways for taurine in HSCs; HSCs: Hepatic stellate cells.

was consistent with the finding of a previous study which showed that taurine can obviously decrease LDL-C level[26].

Moreover, amino-dodecanoic acid, 2-oxo-4-methylthiobutanoic acid, oxo-dodecenoic acid, valine, citric acid, thiamine, and N-acetylaspartate were also identified in the current study. It is therefore proposed that taurine may intervene HSCs through the valine, leucine and isoleucine biosynthesis pathway, cysteine and methionine metabolism pathway, citrate cycle (TCA cycle) pathway, alanine, aspartate and glutamate metabolism pathway, lysine degradation pathway, glyo-

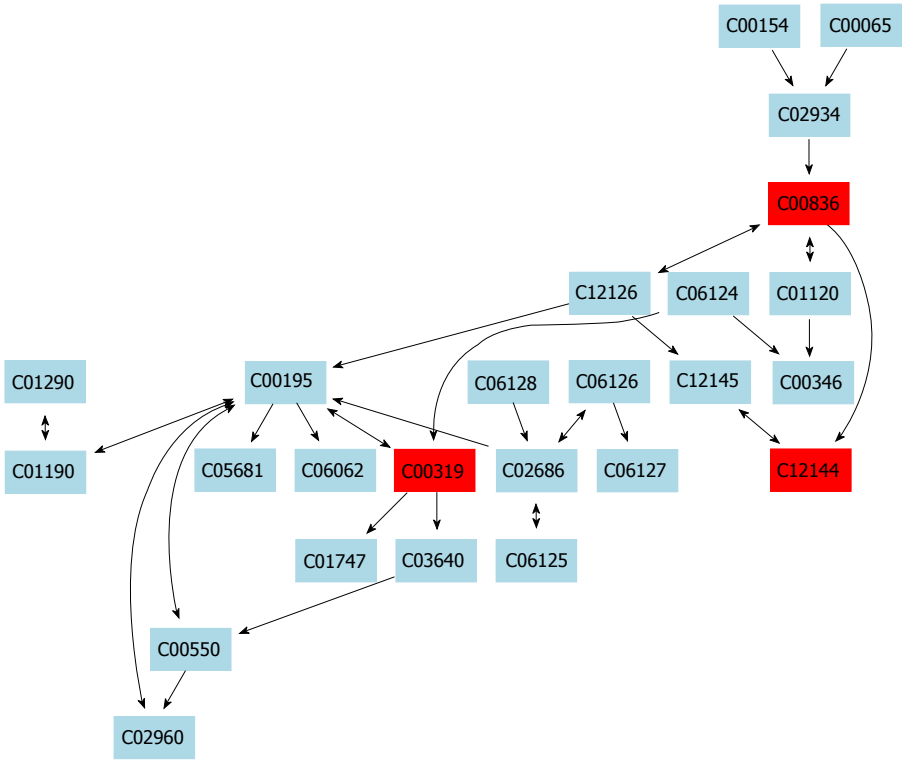

Figure 4 Sphingolipid metabolism pathway.

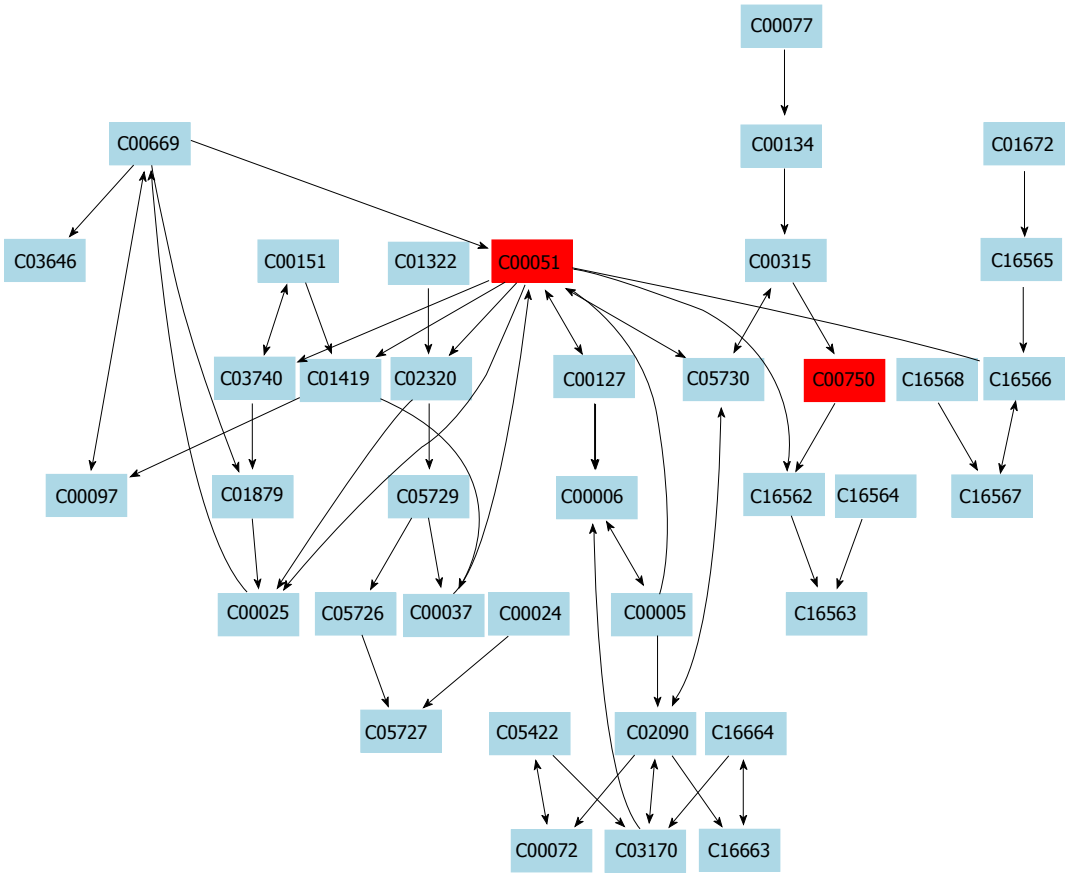

Figure 5 Glutathione metabolism pathway.

xylate and dicarboxylate metabolism pathway, arginine and proline metabolism pathway and aminoacyl-tRNA

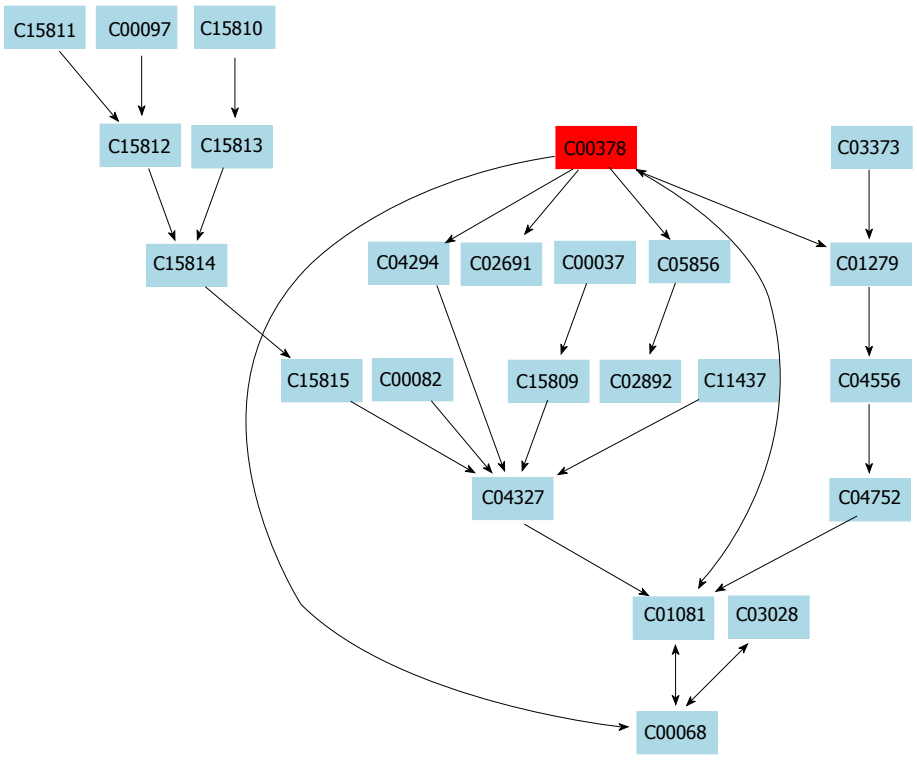

Figure 6 Thiamine metabolism pathway.

biosynthesis pathway.

This study has several limitations. Validation of this current chromatography method using targeted metabolomics and application of this current chromatography method on other cell lines or *in vivo* models need to be studied in the future. In addition, dose-dependence of taurine should be clarified in the future.

To conclude, this study has found that there were distinct changes in the biological metabolites of taurine in HSCs by using HPLC-ESI/Q-TOF-MS. A total of 32 significant differential endogenous metabolites and 3 differential metabolic pathways including sphingolipid pathway, glutathione pathway and thiamine metabolism pathway (Figure 6) were identified, which might be of key importance in mediating the mechanism of action of taurine in HSCs.

COMMENTS

Background

It is well-known that quiescent hepatic stellate cells (HSC) may become matrix-secreting myofibroblasts upon activation and are the primary sources of extracellular matrix (ECM) during liver fibrogenesis. Thus, a novel therapeutic method for hepatic fibrosis can rely on the inhibition of activated HSCs. Taurine, a beta-amino acid with a simple structure that is extracted from animal tissue, has been investigated as a promising drug for the treatment of many hepatic injuries. In previous studies, taurine was found to significantly increase the apoptosis of HSCs and raise the concentrations of 19 proteins related to cellular apoptosis or oxidation in HSCs. However, the exact metabolic pathways and molecular mechanisms for taurine are still unknown.

Research frontiers

Metabolomics methods can be used to characterize the metabolic profiles of a biological system. Since metabolites with relatively low molecular weight are downstream products of biological processes, their identity and concentrations in a living biological system can provide biochemical signatures for globally tracking the physiological effects and exploring the drug effects. Therefore, metabolomics methods can be used to identify biomarkers for clinical drug therapy, especially in cancer research.

Innovations and breakthroughs

In this study, a simple chromatography method coupled with pathway analysis by using high-performance liquid chromatography-time electrospray ionization/quadrupole-time of flight mass spectrometry was successfully performed for analyzing the mechanism of action of taurine in HSCs. A total of 32 significantly differential endogenous metabolites were identified, which may mediate the mechanism of action of taurine in HSCs. Among the seven relevant pathways identified for taurine, sphingolipid metabolism pathway, glutathione metabolism pathway and thiamine metabolism pathway were found to be the most important metabolic pathways for taurine in HSCs.

Applications

Taurine, a beta-amino acid with a simple structure that is extracted from animal tissue, has been investigated as a promising drug for the treatment of many hepatic injuries. In previous studies, taurine was found to significantly increase the apoptosis of HSCs and raise the concentrations of 19 proteins related to cellular apoptosis or oxidation in HSCs. However, the exact metabolic pathways and molecular mechanisms for taurine are still unknown. Therefore, this study aimed at developing a reliable and simple method to identify important biological metabolites and relevant pathways for taurine in HSCs, in order to provide more data for taurine therapy.

Terminology

Hepatic fibrosis is a pathological condition characterized by excessive deposition of ECM proteins, which may led to the development of liver cirrhosis or even hepatocellular carcinoma in the absence of effective treatment.

Peer-review

This is an interesting paper looking to identify biological pathways and meta-

bolites for taurine in hepatocytes.

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