

# 水蛭素与缺血性脑卒中

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# 1 摘要

## 1.1 需求

- 复方：地黄 15g、黄芪 15g、葛根 18g、石斛 15g、水蛭 3g、川芎 9g
- 有效成分：水蛭中水蛭素 Hirudin（重点关注）
- 疾病：缺血性脑卒中
- 机制：血管生成
- 目标：找到水蛭素通过 XX 靶点及 XX 靶点涉及的通路 YY 影响缺血性脑卒中的血管生成

请注意，网药有效成分筛选时确认包括水蛭素，如不包括，请及时联系

追加：

- 水蛭素与 CXCL8、CXCR2、CCL2 的分子对接结果

## 1.2 结果

这是以上一份文档（名为：养阴通脑颗粒中关键成分对脑缺血再灌注的影响）为基础修改的 PDF 文档。

# 2 前言

# 3 材料和方法

## 3.1 材料

## 3.2 方法

Mainly used method:

- The `biomart` was used for mapping genes between organism (e.g., `mgc_symbol` to `hgnc_symbol`)<sup>1</sup>.
- R package `ClusterProfiler` used for gene enrichment analysis<sup>2</sup>.
- The Human Gene Database `GeneCards` used for disease related genes prediction<sup>3</sup>.
- Databases of `DisGeNet`, `GeneCards`, `PharmGKB` used for collating disease related targets<sup>3-5</sup>.
- Website `HERB` <http://herb.ac.cn/> used for TCM data source<sup>6</sup>.
- R package `STEINGdb` used for PPI network construction<sup>7,8</sup>.
- The MCC score was calculated referring to algorithm of `CytoHubba`<sup>8</sup>.
- R package `UniProt.ws` used for querying Gene or Protein information.
- R version 4.3.3 (2024-02-29); Other R packages (eg., `dplyr` and `ggplot2`) used for statistic analysis or data visualization.

4 分析结果

5 结论

6 附：分析流程

6.1 养阴通脑颗粒

6.1.1 成分

Table 1 (下方表格) 为表格 Herbs information 概览。

(对应文件为 Figure+Table/Herbs-information.xlsx)

注：表格共有 6 行 18 列，以下预览的表格可能省略部分数据；含有 6 个唯一 ‘Herb\_’；含有 6 个唯一 ‘Herb\_pinyin\_name’。

Table 1: Herbs information

Herb_	Herb_p...	Herb_c...	Herb_e...	Herb_l...	Proper...	Meridians	UsePart	Function	Indica...
HERB00...	CHUAN ...	川芎	Chuanx...	Radix ...	Warm; ...	Liver;...	rhizome	1. To ...	Cerebr...
HERB00...	DI HUANG	地黄	Radix ...	NA	NA	NA	NA	NA	NA
HERB00...	GE GEN	葛根	root o...	Radix ...	Cool; ...	Spleen...	tuberoid	To rel...	Angina...
HERB00...	HUANG QI	黄芪	root o...	Radix ...	Warm; ...	Lung; ...	root	To rei...	Common...
HERB00...	SHI HU	石斛	Dendro...	Herba ...	Minor ...	Stomac...	Dendro...	Treatm...	1. Den...
HERB00...	SHUI ZHI	水蛭	Bigflo...	Garden...	Mild; ...	Liver	fruit	To cle...	Heat t...

Table 2 (下方表格) 为表格 Components of Herbs 概览。

(对应文件为 Figure+Table/Components-of-Herbs.xlsx)

注：表格共有 725 行 4 列，以下预览的表格可能省略部分数据；含有 6 个唯一 ‘herb\_id’；含有 696 个唯一 ‘Ingredient.name’。

Table 2: Components of Herbs

herb_id	Ingredient.id	Ingredient.name	Ingredient.alias
HERB002560	HBIN001244	13-hydroxy-9,11-o...	NA
HERB002560	HBIN002016	1,7-Dihydroxy-3,9...	1,7-dihydroxy-3,9...
HERB002560	HBIN003405	20-Hexadecanoylin...	20-hexadecanoylin...
HERB002560	HBIN003436	20(r)-21,24-cyclo...	20(r)-21,24-cyclo...
HERB002560	HBIN004319	2',4' -...	2', 4'-...
HERB002560	HBIN005731	2'-hydroxy-3	NA

herb_id	Ingredient.id	Ingredient.name	Ingredient.alias
HERB002560	HBIN005735	2'-hydroxy-3...	NA
HERB002560	HBIN005744	2-hydroxy-3-metho...	NA
HERB002560	HBIN006143	2-Nonyl acetate	ANW-21203; SCHEMB...
HERB002560	HBIN006743	(2S)-4-methoxy-7-...	(2S)-4-methoxy-7-...
HERB002560	HBIN007657	3,5-dimethoxystil...	78916-49-1; TR-03...
HERB002560	HBIN007848	3,9-di-O-methylni...	NA
HERB002560	HBIN008647	3-Hydroxy-2-picoline	BTB 09012; 3-Hydr...
HERB002560	HBIN008667	3'-hydroxy-4...	NA
HERB002560	HBIN008668	3'-Hydroxy-4...	3-(3-hydroxy-4-me...
...	...	...	...

### 6.1.2 成分靶点

#### 6.1.2.1 GeneCards 获取化合物靶点

HERBs 数据库包含的 Hirudin 靶点较少：

bindingdb, drugbank, 以及预测工具 Super-Pred 等都难以获取更多关于 hirudin 靶点信息。因此，这里使用 GeneCards 搜索。

Table 3 (下方表格) 为表格 Hirudin targets from GeneCards 概览。

(对应文件为 **Figure+Table/Hirudin-targets-from-GeneCards.xlsx**)

注：表格共有 45 行 7 列，以下预览的表格可能省略部分数据；含有 45 个唯一 ‘Symbol’。

**The GeneCards data was obtained by querying :**

hirudin

**Restrict (with quotes) :**

FALSE

**Filtering by Score: :**

Score > 0

**Advance search: :**

[compounds] ( hirudin )

Table 3: Hirudin targets from GeneCards

Symbol	Description	Category	UniProt_ID	GIFtS	GC_id	Score
F2	Coagulatio...	Protein Co...	P00734	59	GC11P047736	2.58
F2R	Coagulatio...	Protein Co...	P25116	55	GC05P076716	2.23
F10	Coagulatio...	Protein Co...	P00742	59	GC13P113122	1.76
FGA	Fibrinogen...	Protein Co...	P02671	58	GC04M154583	1.76
PLAT	Plasminoge...	Protein Co...	P00750	58	GC08M042174	1.76
F3	Coagulatio...	Protein Co...	P13726	54	GC01M094873	1.76
PLG	Plasminogen	Protein Co...	P00747	58	GC06P160702	1.59
CPA1	Carboxypep...	Protein Co...	P15085	51	GC07P130380	1.12
PLAU	Plasminoge...	Protein Co...	P00749	60	GC10P073909	0.64
CD40LG	CD40 Ligand	Protein Co...	P29965	59	GC0XP136649	0.64
SERPINC1	Serpin Fam...	Protein Co...	P01008	59	GC01M174949	0.64
SERPINE1	Serpin Fam...	Protein Co...	P05121	59	GC07P101127	0.64
TBXA2R	Thromboxan...	Protein Co...	P21731	59	GC19M003594	0.64
CCL2	C-C Motif ...	Protein Co...	P13500	58	GC17P034255	0.64
CD55	CD55 Molec...	Protein Co...	P08174	58	GC01P207321	0.64
...	...	...	...	...	...	...

### 6.1.2.2 所有靶点

Table 4 (下方表格) 为表格 tables of Herbs compounds and targets 概览。

(对应文件为 **Figure+Table/tables-of-Herbs-compounds-and-targets.xlsx**)

注：表格共有 13446 行 9 列，以下预览的表格可能省略部分数据；含有 696 个唯一 ‘Ingredient.id’；含有 6 个唯一 ‘Herb\_pinyin\_name’；含有 696 个唯一 ‘Ingredient.name’；含有 2879 个唯一 ‘Target.name’。

Table 4: Tables of Herbs compounds and targets

Ingred.....1	Herb_p...	Ingred.....3	Ingred.....4	Target.id	Target...	Databa...	Paper.id	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	ATIC	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	FPGS	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	GART	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	MTHFD1	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	MTHFD2	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	ALDH1L1	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	MTHFD1L	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	MTFMT	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	ALDH1L2	NA	NA	...
HBIN00...	SHI HU	10,12-...	NA	HBTAR0...	MTHFD2L	NA	NA	...

Ingred.....1	Herb_p...	Ingred.....3	Ingred.....4	Target.id	Target...	Databa...	Paper.id	...
HBIN00...	SHI HU	10 ,13...	NA	NA	NA	NA	NA	...
HBIN00...	CHUAN ...	10-(be...	10-( -...	NA	NA	NA	NA	...
HBIN00...	CHUAN ...	1,1-Di...	3658-9...	NA	NA	NA	NA	...
HBIN00...	CHUAN ...	1,2,3,...	NA	NA	NA	NA	NA	...
HBIN00...	CHUAN ...	1,3,8-...	1,3,8-...	HB TAR0...	ACHE	NA	NA	...
...	...	...	...	...	...	...	...	...

### 6.1.3 脑缺血再灌注 cerebral ischemia reperfusion (CIR) 靶点

取下方数据集的合集：

Figure 1 (下方图) 为图 Overall targets number of datasets 概览。

(对应文件为 [Figure+Table/Overall-targets-number-of-datasets.pdf](#))

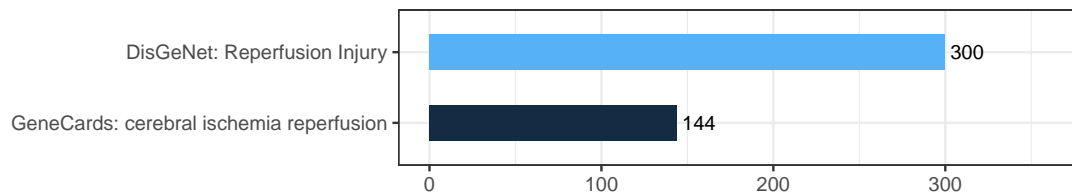


Figure 1: Overall targets number of datasets

### 6.1.4 网络药理-疾病

Figure 2 (下方图) 为图 Network pharmacology with disease 概览。

(对应文件为 [Figure+Table/Network-pharmacology-with-disease.pdf](#))



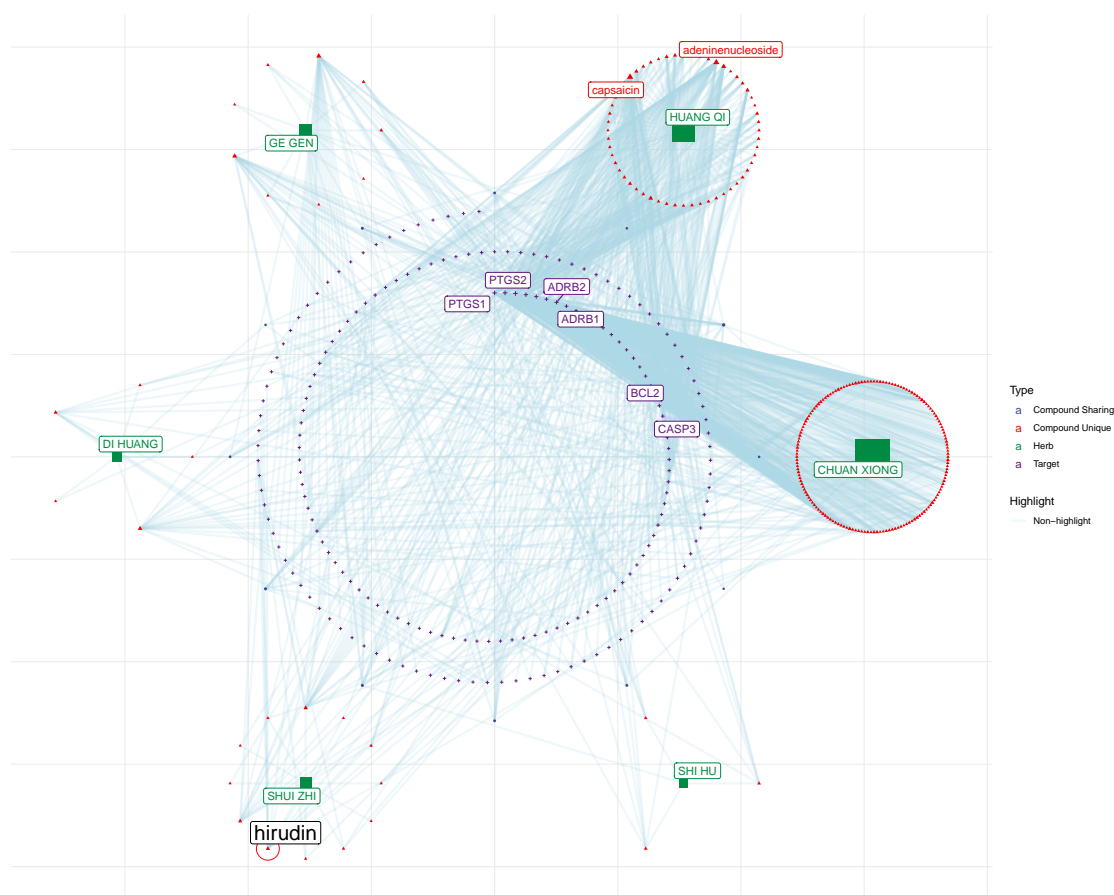


Figure 2: Network pharmacology with disease

Figure 3 (下方图) 为图 Targets intersect with targets of diseases 概览。

(对应文件为 `Figure+Table/Targets-intersect-with-targets-of-diseases.pdf`)

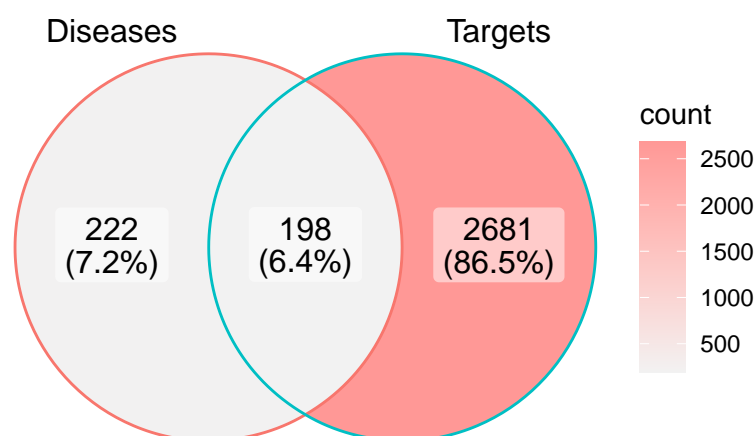


Figure 3: Targets intersect with targets of diseases

**Intersection :**

IL10, HMOX1, MMP9, PTGS2, SOD2, MPO, NOS2, IL6, CAT, CXCL2, TLR4, ALOX5, RELA, CCL2, CASP3, SELE, XDH, FOS, EDN1, TLR2, PLAT, PTEN, MAPK8, PPARA, CDKN1A, KDR, ADORA2A, CXCL1, PLA2, BCL2, SOD1, PPARG, NOS3, TNF, IL1B, MAPK9, ICAM1, THBS1, TERT, JUN, ADORA2B, EFNB2, HGF, CD36, IRAK3, SLPI, IL12A, C...

(上述信息框内容已保存至 `Figure+Table/Targets-intersect-with-targets-of-diseases-content`)

### 6.1.5 PPI 网络

Figure 4 (下方图) 为图 HERBS raw PPI network 概览。

(对应文件为 `Figure+Table/HERBS-raw-PPI-network.pdf`)

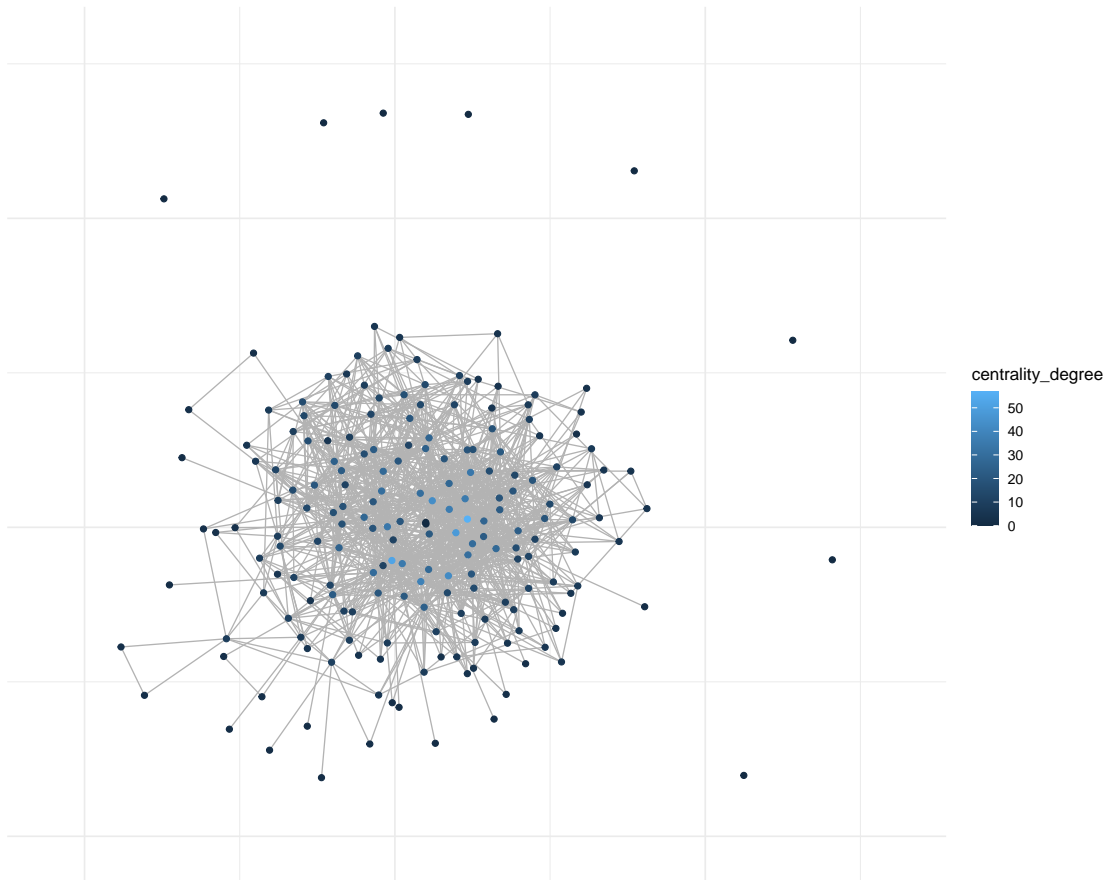


Figure 4: HERBS raw PPI network

Figure 5 (下方图) 为图 HERBS Top30 MCC score 概览。

(对应文件为 `Figure+Table/HERBS-Top30-MCC-score.pdf`)

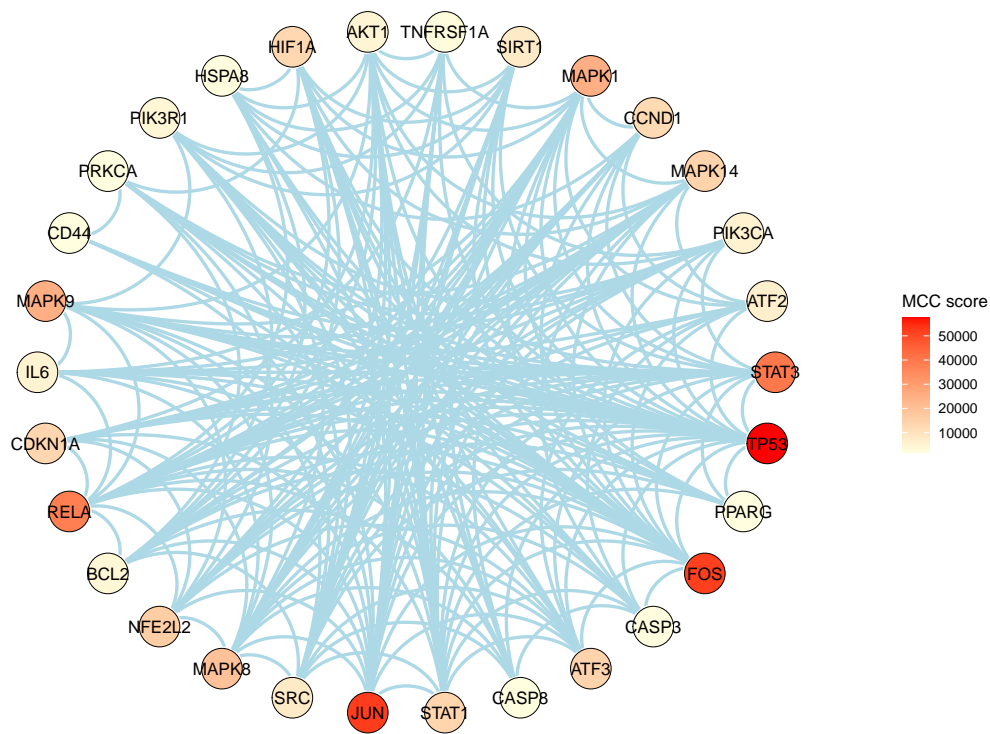


Figure 5: HERBS Top30 MCC score

### 6.1.6 富集分析 (Top30)

Figure 6 (下方图) 为图 HERBS KEGG enrichment 概览。

(对应文件为 `Figure+Table/HERBS-KEGG-enrichment.pdf`)

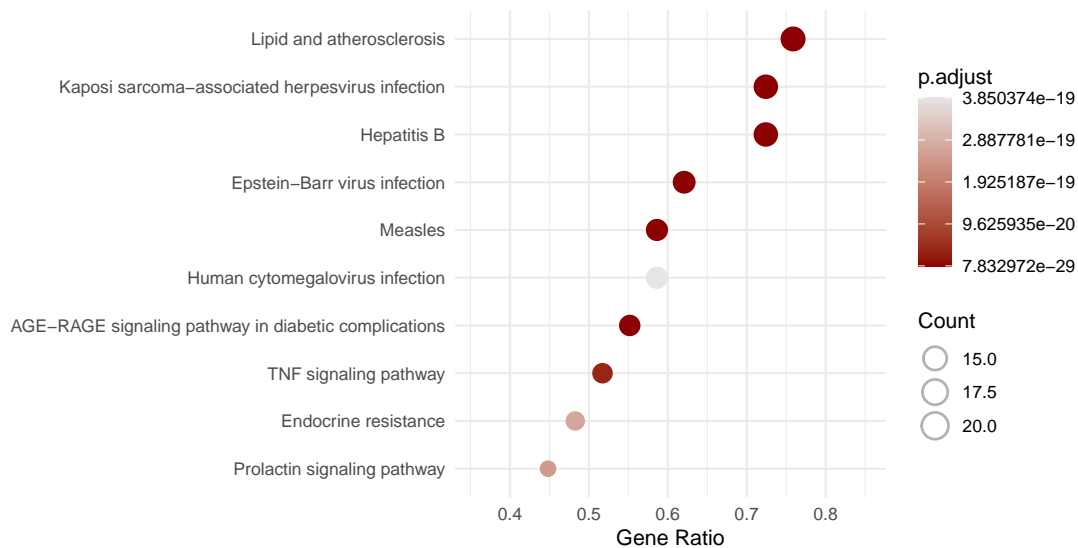


Figure 6: HERBS KEGG enrichment

Table 5 (下方表格) 为表格 HERBS KEGG enrichment data 概览。

(对应文件为 Figure+Table/HERBS-KEGG-enrichment-data.xlsx)

注：表格共有 195 行 9 列，以下预览的表格可能省略部分数据；含有 195 个唯一 ‘ID’。

1. pvalue: 显著性 P。

Table 5: HERBS KEGG enrichment data

ID	Descri...	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
hsa05161	Hepati...	21/29	162/8764	4.0169...	7.8329...	1.1416...	207/13...	21
hsa05417	Lipid ...	22/29	215/8764	1.7025...	1.6599...	2.4194...	207/59...	22
hsa05167	Kaposi...	21/29	194/8764	2.1692...	1.4099...	2.0550...	207/83...	21
hsa04933	AGE-RA...	16/29	100/8764	1.4213...	6.9289...	1.0098...	207/59...	16
hsa05162	Measles	17/29	138/8764	3.6237...	1.4132...	2.0598...	207/59...	17
hsa05169	Epstei...	18/29	202/8764	4.3574...	1.4161...	2.0640...	207/59...	18
hsa04668	TNF si...	15/29	114/8764	1.3331...	3.7136...	5.4126...	207/13...	15
hsa04917	Prolac...	13/29	70/8764	1.0206...	2.4877...	3.6258...	207/59...	13
hsa01522	Endocr...	14/29	98/8764	1.2349...	2.6756...	3.8997...	207/59...	14
hsa05163	Human ...	17/29	225/8764	1.9745...	3.8503...	5.6118...	207/13...	17
hsa05210	Colore...	13/29	86/8764	1.8209...	3.2280...	4.7048...	207/59...	13
hsa04210	Apoptosis	14/29	135/8764	1.3592...	2.2088...	3.2193...	207/59...	14
hsa05142	Chagas...	13/29	102/8764	1.9039...	2.8558...	4.1623...	207/84...	13
hsa05418	Fluid ...	14/29	139/8764	2.0751...	2.8903...	4.2126...	207/59...	14
hsa04625	C-type...	13/29	104/8764	2.4816...	3.2261...	4.7020...	207/84...	13
...	...	...	...	...	...	...	...	...

Table 6 (下方表格) 为表格 Compounds contributes to Top30 概览。

(对应文件为 Figure+Table/Compounds-contributes-to-Top30.xlsx)

注：表格共有 291 行 3 列，以下预览的表格可能省略部分数据；含有 6 个唯一 ‘Herb\_pinyin\_name’；含有 106 个唯一 ‘Ingredient.name’；含有 30 个唯一 ‘Target.name’。

Table 6: Compounds contributes to Top30

Herb_pinyin_name	Ingredient.name	Target.name
HUANG QI	13-hydroxy-9,11-octadecadie...	PPARG
HUANG QI	1,7-Dihydroxy-3,9-dimethoxy...	PPARG
HUANG QI	1,7-Dihydroxy-3,9-dimethoxy...	MAPK14

Herb_pinyin_name	Ingredient.name	Target.name
CHUAN XIONG	1-Acetyl-beta-carboline	MAPK14
CHUAN XIONG	1-beta-ethylacrylate-7-alde...	MAPK14
HUANG QI	3,9-di-O-methylnissolin	PPARG
HUANG QI	3,9-di-O-methylnissolin	MAPK14
CHUAN XIONG	3-Butylidene-7-hydroxyphta...	PPARG
CHUAN XIONG	3-butylidene-phalide	CCND1
CHUAN XIONG	3-butylidene-phalide	CDKN1A
CHUAN XIONG	3-butylidene-phalide	TP53
GE GEN	3'-Methoxydaidzein	PPARG
GE GEN	3'-Methoxydaidzein	MAPK14
CHUAN XIONG	4,7-Dihydroxy-3-butylphthalide	PPARG
CHUAN XIONG	4-hydroxy-3-butylphthalide	PPARG
...	...	...

## 6.2 水蛭素 Hirudin

### 6.2.1 水蛭素-靶点-富集通路

Figure 7 (下方图) 为图 Hirudin targets of disease 概览。

(对应文件为 `Figure+Table/Hirudin-targets-of-disease.pdf`)

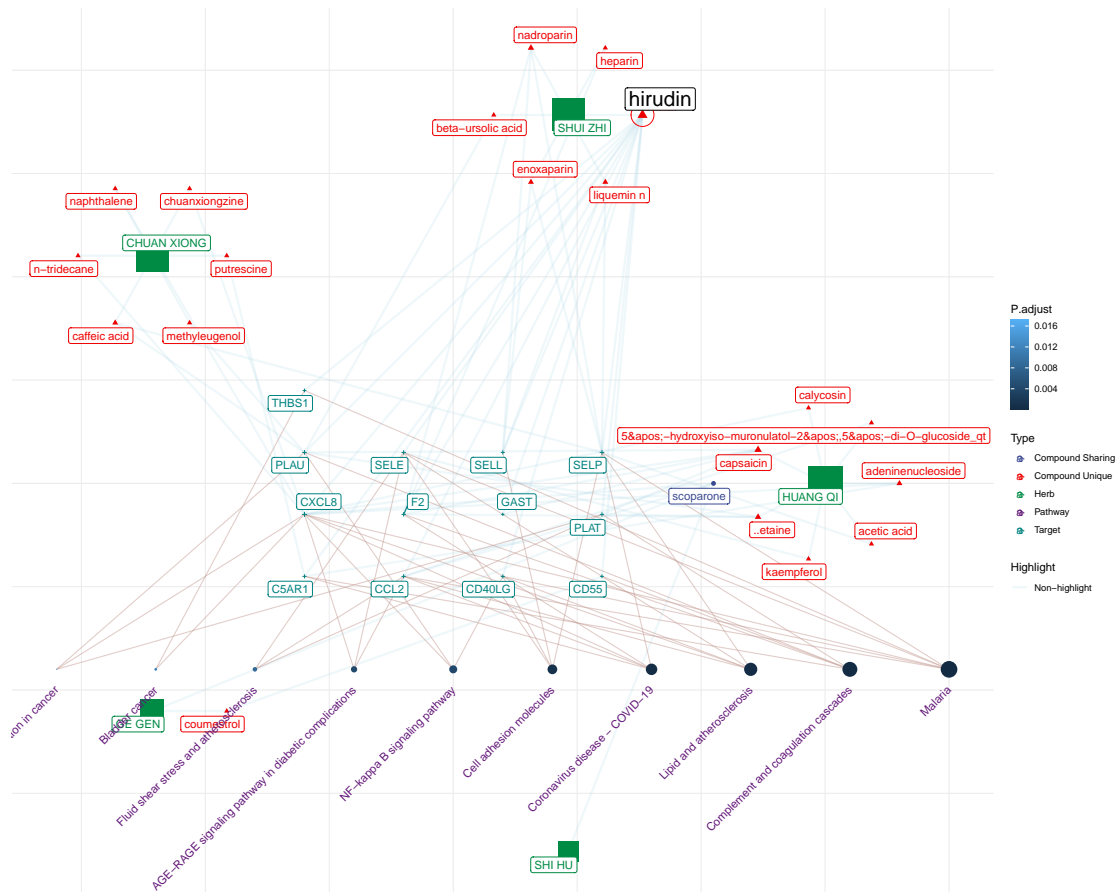


Figure 7: Hirudin targets of disease

Figure 8 (下方图) 为图 HIRU KEGG enrichment 概览。

(对应文件为 Figure+Table/HIRU-KEGG-enrichment.pdf)

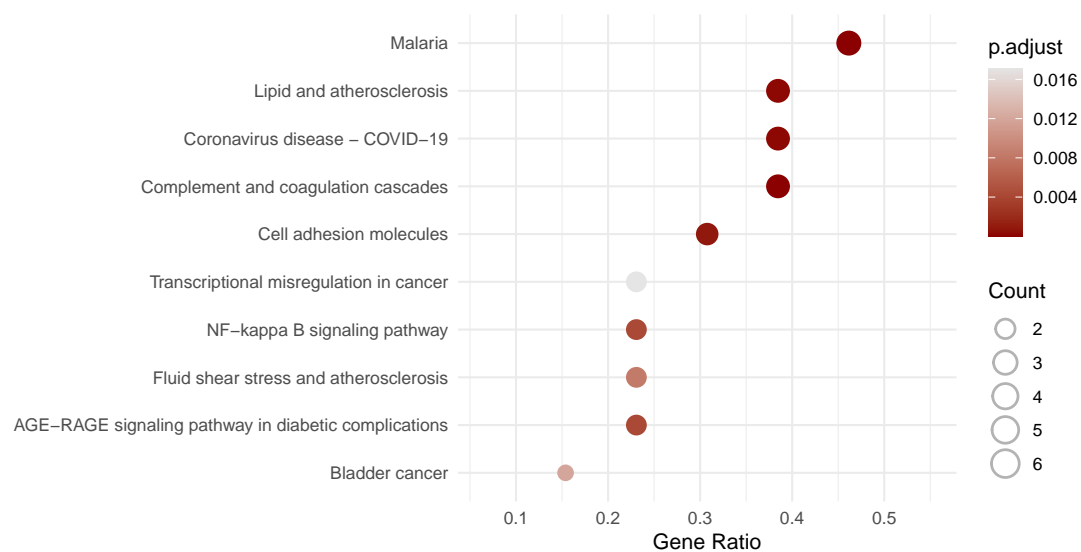


Figure 8: HIRU KEGG enrichment

Figure 9 (下方图) 为图 HIRU GO enrichment 概览。

(对应文件为 **Figure+Table/HIRU-GO-enrichment.pdf**)

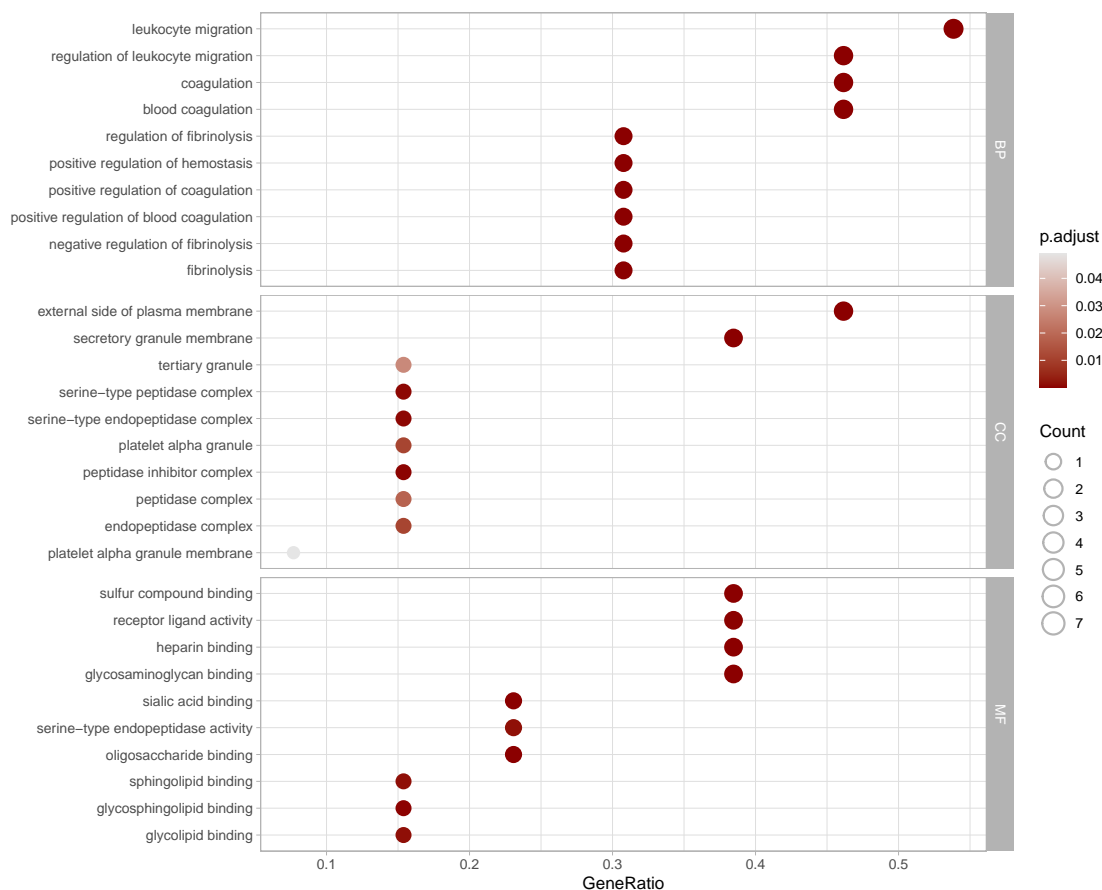


Figure 9: HIRU GO enrichment

## 6.2.2 分子对接

## Reference

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