Supplementary

Table S1 The search strategy

Search number	Query	Results
The search strategy (PubMed)		
1	Astragalus Plant[MeSH Terms]	2440
2	"Astragalus Plant*"[Title/Abstract] OR "Milk Vetch*"[Title/Abstract] OR "Wooly Locoweed*"[Title/Abstract] OR "Astragalus Polysaccharide"[Title/Abstract] OR "Astragaloside"[Title/Abstract] OR "Astragalus Flavone"[Title/Abstract] OR "Astragalus Membranaceus"[Title/Abstract] OR "Astragalus mongholicus"[Title/Abstract]	3123
3	Liver Neoplasms[MeSH Terms]	200870
4	"Adult Liver Cancer*"[Title/Abstract] OR "Cancer of Liver"[Title/Abstract] OR "cancer of the liver"[Title/Abstract] OR "carcinomatous liver"[Title/Abstract] OR "hepatic cancer*"[Title/Abstract] OR "hepatic malignanc*"[Title/Abstract] OR "Hepatic Neoplasm*"[Title/Abstract] OR "hepatocellular cancer*"[Title/Abstract] OR "Hepatocellular Carcinoma*"[Title/Abstract] OR "hepatocellular malignanc*"[Title/Abstract] OR "hepatocyte cancer"[Title/Abstract] OR "Hepatoma*"[Title/Abstract] OR "liver cancer*"[Title/Abstract] OR "liver cell cancer"[Title/Abstract] OR "Liver Cell Carcinoma*"[Title/Abstract] OR "liver malignanc*"[Title/Abstract] OR "Liver Neoplasm*"[Title/Abstract] OR "liver primary cancer"[Title/Abstract] OR "malignancies of the liver"[Title/Abstract] OR "malignancy of the liver"[Title/Abstract] OR "malignant hepatic neoplasm"[Title/Abstract] OR "malignant hepatic tumo*"[Title/Abstract] OR "malignant liver neoplasm"[Title/Abstract] OR "malignant liver tumo*"[Title/Abstract] OR "malignant neoplasm of the liver"[Title/Abstract] OR "malignant neoplasms of the liver"[Title/Abstract] OR "malignant tumor of the liver"[Title/Abstract] OR "malignant tumors of the liver"[Title/Abstract] OR "malignant tumour of the liver"[Title/Abstract] OR "malignant tumours of the liver"[Title/Abstract] OR "primary liver cancer"[Title/Abstract]	181231
5	(#1 OR #2) AND (#3 OR #4)	80
The search strategy (Embase)		
1	'astragalus (plant)'/exp	3801
2	'astragalus plant*':ti,ab,kw OR 'milk vetch*':ti,ab,kw OR 'wooly locoweed*':ti,ab,kw OR 'astragalus polysaccharide':ti,ab,kw OR 'astragaloside':ti,ab,kw OR 'astragalus flavone':ti,ab,kw OR 'astragalus membranaceus':ti,ab,kw OR 'astragalus mongholicus':ti,ab,kw	4022
3	'liver cancer'/exp	343519
4	'adult?liver cancer*':ti,ab,kw OR 'cancer of liver':ti,ab,kw OR 'cancer of the liver':ti,ab,kw OR 'carcinomatous liver':ti,ab,kw OR 'hepatic cancer*':ti,ab,kw OR 'hepatic malignanc*':ti,ab,kw OR 'hepatic neoplasm*':ti,ab,kw OR 'hepatocellular cancer*':ti,ab,kw OR 'hepatocellular carcinoma*':ti,ab,kw OR 'hepatocellular malignanc*':ti,ab,kw OR 'hepatocyte cancer':ti,ab,kw OR 'hepatoma*':ti,ab,kw OR 'liver cancer*':ti,ab,kw OR 'liver cell cancer':ti,ab,kw OR 'liver cell carcinoma*':ti,ab,kw OR 'liver malignanc*':ti,ab,kw OR 'liver neoplasm*':ti,ab,kw OR 'liver primary cancer':ti,ab,kw OR 'malignancies of the liver':ti,ab,kw OR 'malignancy of the liver':ti,ab,kw OR 'malignant hepatic neoplasm':ti,ab,kw OR 'malignant hepatic tumo*':ti,ab,kw OR 'malignant liver neoplasm':ti,ab,kw OR 'malignant liver tumo*':ti,ab,kw OR 'malignant neoplasm of the liver':ti,ab,kw OR 'malignant neoplasms of the liver':ti,ab,kw OR 'malignant tumor of the liver':ti,ab,kw OR 'malignant tumors of the liver':ti,ab,kw OR 'malignant tumour of the liver':ti,ab,kw OR 'malignant tumours of the liver':ti,ab,kw OR 'primary liver cancer':ti,ab,kw	251842
5	(#1 OR #2) AND (#3 OR #4)	167
The search strategy (Cochrance)		
1	MeSH descriptor: [Astragalus Plant] explode all trees	115
2	('Astragalus Plant*' OR 'Milk Vetch*' OR 'Wooly Locoweed*' OR 'Astragalus Polysaccharide' OR 'Astragaloside' OR 'Astragalus Flavone' OR 'Astragalus Membranaceus' OR 'Astragalus mongholicus'):ti,ab,kw	267
3	Liver Neoplasms	7124
4	('Adult Liver Cancer*' OR 'Cancer of Liver' OR 'cancer of the liver' OR 'carcinomatous liver' OR 'hepatic cancer*' OR 'hepatic malignanc*' OR 'Hepatic Neoplasm*' OR 'hepatocellular cancer*' OR 'Hepatocellular Carcinoma*' OR 'hepatocellular malignanc*' OR 'hepatocyte cancer' OR 'Hepatoma*' OR 'liver cancer*' OR 'liver cell cancer' OR 'Liver Cell Carcinoma*' OR 'liver malignanc*' OR 'Liver Neoplasm*' OR 'liver primary cancer' OR 'malignancies of the liver' OR 'malignancy of the liver' OR 'malignant hepatic neoplasm' OR 'malignant hepatic tumo*' OR 'malignant liver neoplasm' OR 'malignant liver tumo*' OR 'malignant neoplasm of the liver' OR 'malignant neoplasms of the liver' OR 'malignant tumor of the liver' OR 'malignant tumors of the liver' OR 'malignant tumour of the liver' OR 'malignant tumours of the liver' OR 'primary liver cancer'):ti,ab,kw	21767
5	(#1 OR #2) AND (#3 OR #4)	12
The search strategy (CBM)		
1	("黄芪"[常用字段:智能] OR "黄耆"[常用字段:智能] OR "黄芪多糖"[常用字段:智能] OR "黄芪甲苷"[常用字段:智能] OR "黄芪总苷"[常用字段:智能] OR "黄芪黄酮"[常用字段:智能] OR "黄芪皂苷"[常用字段:智能]) AND("肝癌"[常用字段:智能] OR "肝恶性肿瘤"[常用字段:智能] OR "原发性肝细胞癌"[常用字段:智能] OR "肝脏恶性肿瘤"[常用字段:智能] OR "肝腺癌"[常用字段:智能] OR "肝肿瘤"[常用字段:智能] OR "肝细胞癌"[常用字段:智能])	366
The search strategy (web of science)		
1	((Astragalus Plant*) OR (Milk Vetch*) OR (Wooly Locoweed*) OR (Astragalus Polysaccharide) OR (Astragaloside) OR (Astragalus Flavone) OR (Astragalus Membranaceus) OR (Astragalus mongholicus))	6414
2	((Adult Liver Cancer*) OR (Cancer of Liver) OR (cancer of the liver) OR (carcinomatous liver) OR (hepatic cancer*) OR (hepatic malignanc*) OR (Hepatic Neoplasm*) OR (hepatocellular cancer*) OR (Hepatocellular Carcinoma*) OR (hepatocellular malignanc*) OR (hepatocyte cancer) OR (Hepatoma*) OR (liver cancer*) OR (liver cell cancer) OR (Liver Cell Carcinoma*) OR (liver malignanc*) OR (Liver Neoplasm*) OR (liver primary cancer) OR (malignancies of the liver) OR (malignancy of the liver) OR (malignant hepatic neoplasm) OR (malignant hepatic tumo*) OR (malignant liver neoplasm) OR (malignant liver tumo*) OR (malignant neoplasm of the liver) OR (malignant neoplasms of the liver) OR (malignant tumor of the liver) OR (malignant tumors of the liver) OR (malignant tumour of the liver) OR (malignant tumours of the liver) OR (primary liver cancer))	386871
3	#1 AND #2	162
The search strategy (维普)		
1	黄芪+黄耆+黄芪多糖+黄芪甲苷+黄芪总苷+黄芪黄酮+黄芪皂苷	
2	肝癌+肝恶性肿瘤+原发性肝细胞癌+肝脏恶性肿瘤+肝腺癌+肝肿瘤+肝细胞癌	
3	#1 AND #2	412
The search strategy (CNKI)		
1	黄芪 + 黄耆 + 黄芪多糖 + 黄芪甲苷 + 黄芪总苷 + 黄芪黄酮 + 黄芪皂苷	
2	肝癌 + 肝恶性肿瘤 + 原发性肝细胞癌 + 肝脏恶性肿瘤 + 肝腺癌 + 肝肿瘤 + 肝细胞癌	
3	#1 AND #2	704
The search strategy (万方)		
1	黄芪 OR 黄耆 OR 黄芪多糖 OR 黄芪甲苷 OR 黄芪总苷OR 黄芪黄酮 OR 黄芪皂苷	
2	肝癌 OR 肝恶性肿瘤 OR 原发性肝细胞癌 OR 肝脏恶性肿瘤 OR 肝腺癌 OR 肝肿瘤 OR 肝细胞癌	
3	#1 AND #2	751

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Table S2 GRADE

Certainty assessment							No. of patients		Effect		Certainty
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AM	Placebo	Relative (95% CI)	Absolute (95% CI)	
Question: AM compared to placebo for liver tumor volume											
Low dose AM											
10	Randomised trials	Serious	Serious	Not serious	Not serious	None			-	SMD 5.03 SD fewer (6.95 fewer to 3.1 more)	⊕⊕◯◯ Low
High-dose AM											
9	Randomised trials	Serious	Serious	Not serious	Not serious	None			-	SMD 5.8 SD fewer (8.26 fewer to 3.34 fewer)	⊕⊕◯◯ Low
Question: AM compared to placebo for tumor weight											
Low dose AM											
22	Randomised trials	Not serious	Serious	Not serious	Serious	None	251	251	-	SMD 2.14 SD lower (2.77 lower to 1.52 lower)	⊕⊕◯◯ Low
High-dose AM											
11	Randomised trials	Not serious	Serious	Not serious	Serious	None	96	95	-	SMD 2.71 SD lower (3.53 lower to 1.89 lower)	⊕⊕◯◯ Low
Question: AM compared to placebo for liver function											
ALT											
6	Randomised trials	Not serious	Not serious	Serious	Serious	None	73	83	-	SMD 3.95 SD lower (6.13 lower to 1.78 lower)	⊕⊕◯◯ Low
AST											
5	Randomised trials	Not serious	Not serious	Serious	Serious	None			-	SMD 5.91 SD lower (9 lower to 2.82 lower)	⊕⊕◯◯ Low
ALP											
3	Randomised trials	Not serious	Not serious	Not serious	Serious	None	35	45	-	SMD 0.69 SD lower (1.8 lower to 0.42 lower)	⊕⊕⊕◯ Moderate
IL-2											
8	Randomised trials	Not serious	Not serious	Serious	Serious	None	68	68	-	SMD 2.88 SD higher (1.38 higher to 4.37 higher)	⊕⊕◯◯ Low
IL-6											
5	Randomised trials	Not serious	Not serious	Serious	Serious	None	63	63	-	SMD 0.93 SD higher (2.05 lower to 3.91 higher)	⊕⊕◯◯ Low
IFN-γ											
4	Randomised trials	Not serious	Not serious	Serious	Serious	None	35	45	-	SMD 4.67 SD higher (1.63 higher to 7.7 higher)	⊕⊕◯◯ Low
TNF-α											
11	Randomised trials	Not serious	Not serious	Serious	Serious	None	118	118	-	SMD 2 SD higher (0.66 higher to 3.33 higher)	⊕⊕◯◯ Low
Thymus index											
12	Randomised trials	Serious	Not serious	Not serious	Serious	None	146	146	-	SMD 1.42 SD higher (0.66 higher to 2.18 higher)	⊕⊕◯◯ Low
Spleen index											
11	Randomised trials	Not serious	Not serious	Not serious	Serious	None	136	136	-	SMD 0.81 SD higher (0.11 lower to 1.74 higher)	⊕⊕⊕◯ Moderate
Bax											
3	Randomised trials	Not serious	Not serious	Not serious	Serious	None	21	21	-	SMD 2.89 SD higher (0.7 higher to 5.07 higher)	⊕⊕⊕◯ Moderate
Bcl-2											
4	Randomised trials	Not serious	Not serious	Not serious	Serious	None	21	20	-	SMD 3.1 SD lower (5.89 lower to 0.31 lower)	⊕⊕⊕◯ Moderate
MMP-2											
3	Randomised trials	Not serious	Not serious	Not serious	Serious	None	33	34	-	SMD 3.42 SD lower (6.83 lower to 0.02 lower)	⊕⊕⊕◯ Moderate

CI, confidence interval; SMD, standardised mean difference.

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Table S3 The subgroup analysis of main active ingredients of AM on tumor volume, tumor weight, ALT, AST, spleen index and thymus index

Parameter	Subgroup	Effect size	No. studies	SMD [95% CI]	I^2
Tumor volume	Year	Before 2019	7	−2.7 [−3.39, −2.00]	93%
		After 2019	10	−2.63 [−3.24, −2.02]	88%
	Administration route	ig	8	−1.76 [−2.31, −1.21]	91%
		Injection	9	−2.21 [−2.80, −1.62]	91%
	Type	As-IV	6	−2.13 [−2.80, −1.46]	89%
		APS	5	−2.74 [−3.62, −1.86]	77%
		Astragalus	4	−1.04 [−1.77, −0.30]	96%
	Duration	≤2w	9	−4.92 [−7.01, −2.83]	91%
		>2w	8	−5.36 [−7.28, −2.98]	91%
Tumor weight	Year	Before 2019	18	−1.81 [−2.31, −1.31]	77%
		After 2019	12	− 4.64 [−6.39, −2.88]	88%
	Administration route	ig	18	−2.43 [−3.22, −1.63]	86%
		Injection	12	−2.57 [−3.43, −1.07]	79%
	Type	As-IV	6	−3.54 [−5.70, −1.37]	89%
		APS	13	−2.30 [−3.27, −1.33]	88%
		Astragalus	9	− 2.29 [−3.02, −1.55]	39%
		TSA	2	−3.04 [−7.80,1.72]	94%
	Duration	≤2w	20	−2.40 [−2.93, −1.75]	82%
		>2w	10	−2.76 [−4.14, −1.38]	85%
ALT	Year	Before 2019	4	−1.23 [−1.73, −0.73]	96%
		After 2019	2	−3.72 [−4.90, −2.54]	0%
	Administration route	ig	5	−4.84[−7.86, −1.82]	95%
		Injection	1	−0.58[−1.31,0.15]	–
	Type	AS	8	−2.86 [−3.95, −1.76]	82%
		ASTs	1	−0.58 [−1.31, 0.15]	–
		Astragalus	1	−3.30 [−4.74, −1.86]	–
		APS	2	−1.32 [−2.07, −0.57]	98%
	Duration	≤2w	4	−3.85 [−6.69, −1.02]	96%
		>2w	2	−3.85 [−5.55, −2.96]	0%
AST	Year	Before 2019	4	−1.23 [−1.73, −0.73]	76%
		After 2019	2	−3.34 [−4.90, −2.54]	45%
	Administration route	ig	4	−3.67 [−4.54, −2.79]	44.7%
		Injection	1	−1.21 [−2.00, −0.43]	–
	Type	As-IV	2	−2.53 [−3.47, −1.59]	7%
		APS	1	−19.32[−23.82, −14.8]	–%
		Astragalus	2	−1.68 [−2.44, −0.92]	95%
	Duration	≤2 w	4	−3.85[−6.69, −1.02]	96%
		>2 w	2	−4.26 [−5.55, −2.96]	0%
Spleen index	Year	Before 2019	8	0.47 [−0.63, 1.57]	92%
		After 2019	3	1.99 [−0.09, 4.07]	86%
	Administration route	ig	5	−4.84[−7.86, −1.82]	95%
		Injection	1	−0.58[−1.31,0.15]	–
	Type	As-IV	2	0.14 [−0.48, 0.76]	0%
		APS	4	0.33 [−2.12, 2.77]	95%
		Astragalus	8	−2.86 [−3.95, −1.76]	82%
		AF	1	0.74 [0.21, 1.26]	–
	Duration	≤2 w	9	0.70 [−0.36, 1.76]	91%
		>2 w	2	1.38 [−1.06, 3.81]	90%
Thymus index	Year	Before 2019	8	0.74 [0.45, 1.03]	81%
		After 2019	3	2.22 [1.46, 1.03]	70%
	Administration route	ig	9	1.21[0.47,1.96]	83%
		Injection	2	0.66[−1.26,2.57]	81%
	Type	As-IV	2	0.15 [−0.72, 1.01]	47%
		APS	4	1.04 [−0.26, 2.33]	85%
		Astragalus	4	1.87 [0.18, 3.56]	88%
		AF	1	1.03 [0.49, 1.57]	–
	Duration	≤2 w	9	0.98 [0.21, 1.76]	84%
		>2 w	2	1.73 [0.98, 2.48]	82%

Due to the high heterogeneity among the studies, we conducted subgroup analyses on the effects of tumor volume, tumor weight, ALT, AST, spleen index, and thymus index based on the publication year, the type of the main active component of AM, the administration route of the main active component of AM, and the treatment duration. The results indicated that the type of the main active component of Coptis chinensis might be the source of the heterogeneity in tumor weight and aspartate aminotransferase, while the other subgroups did not reveal the source of the heterogeneity in transaminase. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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