

Development of drug-induced gastrointestinal injury models based on ANN and SVM algorithms and its applications in the field of Natural Products

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[#]These authors contributed equally to this work and should be considered co-first authors

*Correspondence: Yaqi Yao and Yubo li

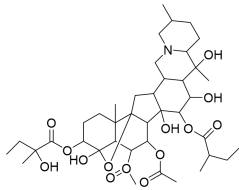
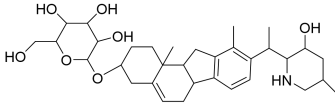
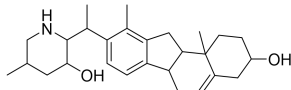
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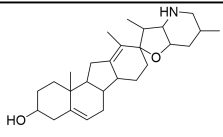
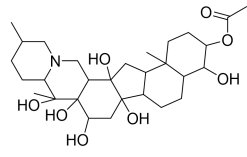
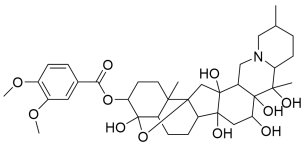
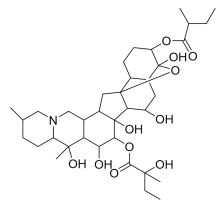
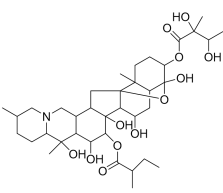
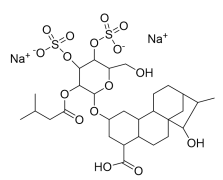
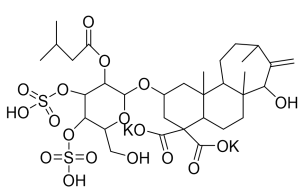
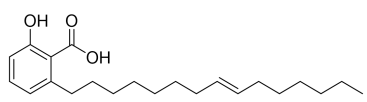
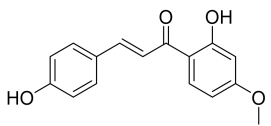
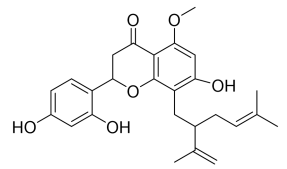
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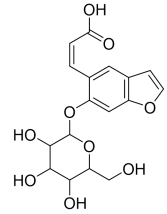
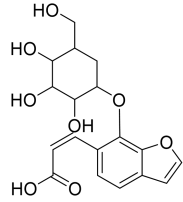
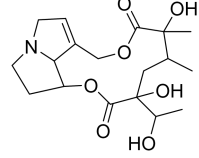
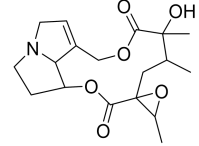
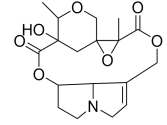
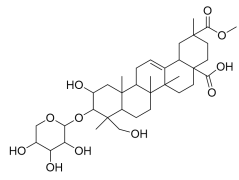
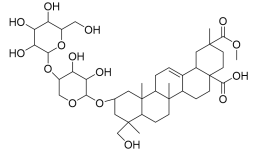
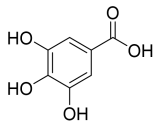
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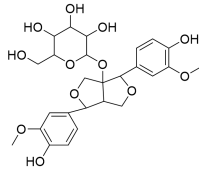
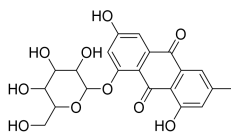
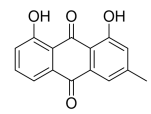
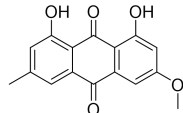
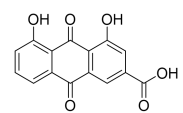
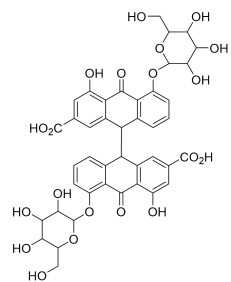
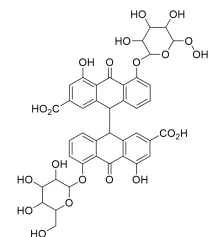
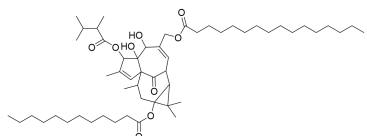
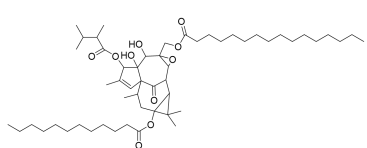
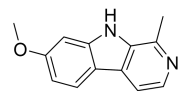
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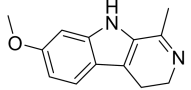
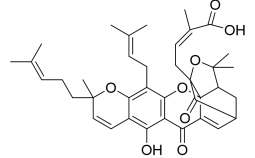
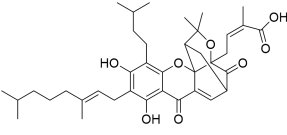
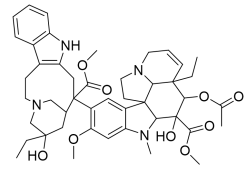
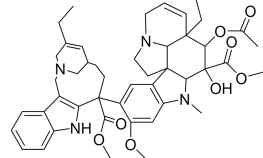
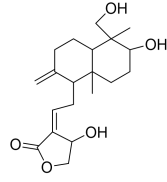
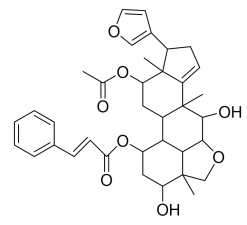
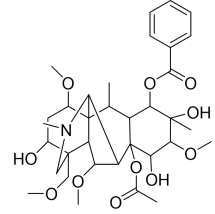
Table S1. Screening of DIGI components of natural products based on ANN model

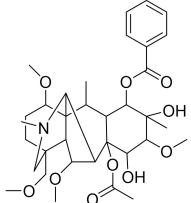
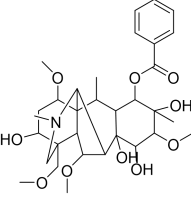
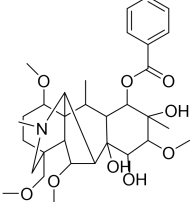
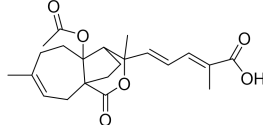
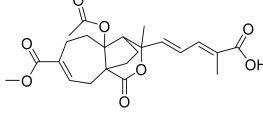
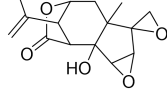
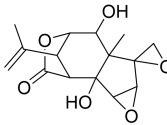
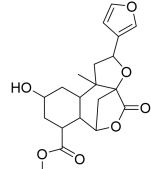
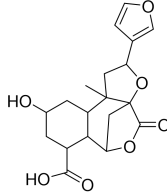
herbs	components	Compound structure
	Protoveratrine A	
Veratrum nigrum	Veratrosine	
	Veratramine	

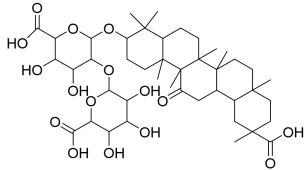
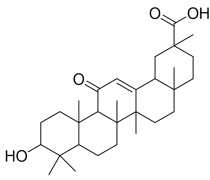
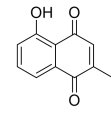
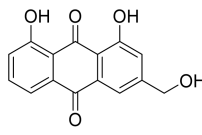
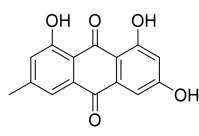
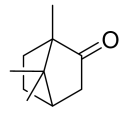
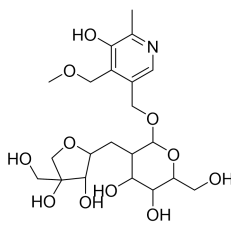
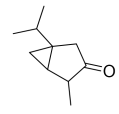
herbs	components	Compound structure
	Cyclopamine	
	Veratrine	
	Veratridine	
	Germerine	
	Neogermbudine	
Xanthii Fructus	Atractyloside	
	Carboxyatractyloside	
Ginkgo Semen	Ginkgolic acid	
	4'-O-Methylpyridoxine	
Radix Sophorae Flavescentis	Kurarinone	

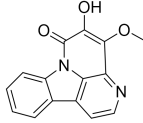
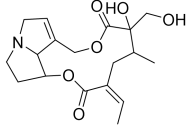
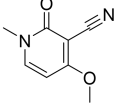
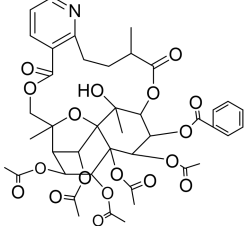
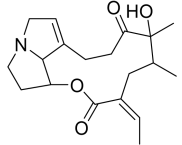
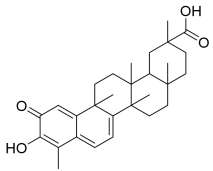
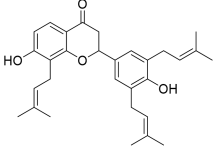
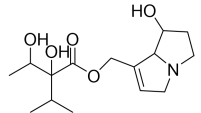
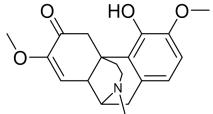

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Psoraleae Fructus	Psoralenoside	
	Isopsoralenoside	
	Jacoline	
Scandentis Hebra	Jacobine	
	Adonifoline	
	Phytolaccae Radix	Esculentoside A
Esculentoside B		
Esculentoside C		
Polygoni Multiflori Radix	Gallic acid	

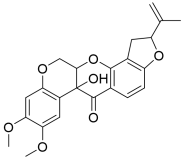
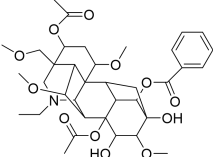
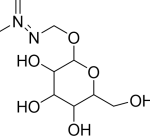
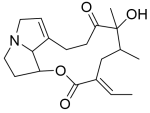
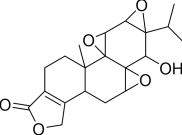
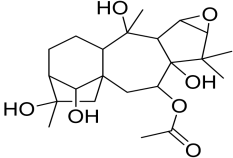
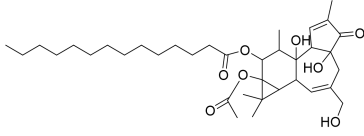
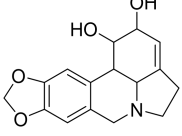
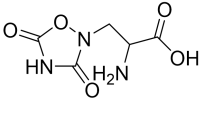
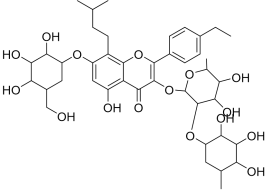
herbs	components	Compound structure
	Emodin- 8- O- glucoside	
	Emodin-8-O- β -D-glucopyranoside	
Rhei radix et rhizoma、Polygoni Multiflori Radix	Chrysophanol	
	Physcion	
	Rhein	
Sannae Folium	Sennoside A	
	Sennoside B	
Kansui Radix	Kansuiphorin A	
	Kansuiphorin B	
Herb Of Common Peganum	Harmine	

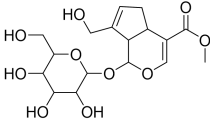
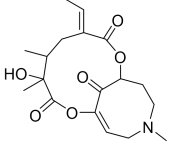
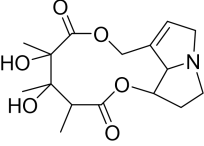
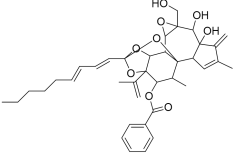
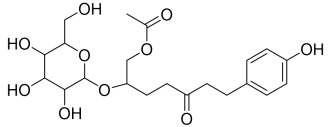
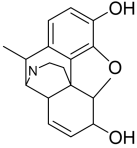
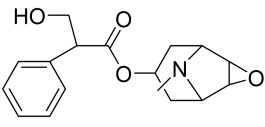
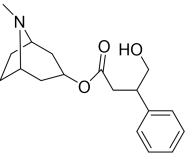
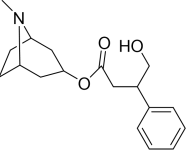
herbs	components	Compound structure
	Harmaline	
Gamboge	Gambogic acid	
	Gambogenic acid	
Catharanthus roseus L.	Vinblastine	
	Vinorelbine	
Andrographis Herba	Andrographolide	
Toosendan Fructus	Trichilin D	
Aconiti Lateralis Radix Praeparata、 Aconiti Radix、 Aconiti	Mesaconitine	

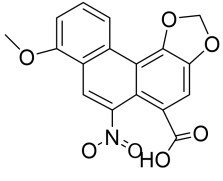
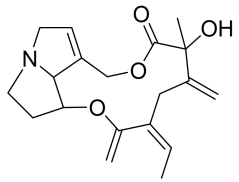
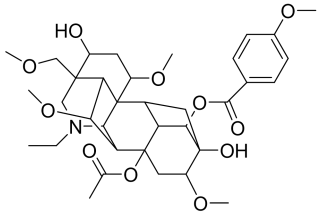
herbs	components	Compound structure
Kusnezoffii Radix、 Aconitum brachypodum Diels	Hypaconitine	
Aconiti Lateralis Radix Praeparata、 Aconiti Radix	Benzoylmesaconine	
	Benzoylhypacoitine	
Pseudolaricis Cortex	Pseudolaric acid A	
	Pseudolaric acid B	
Chinese Coriaria	Coriamyrtin	
	Tutin	
Dioscorea bulbifera	Diosbulbin A	
	Diosbulbin C	

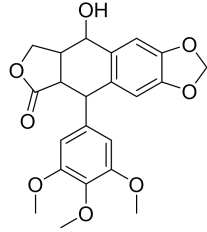
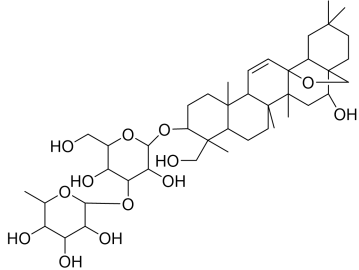
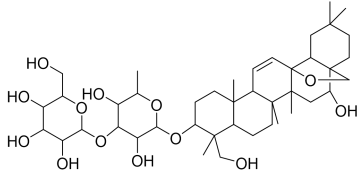
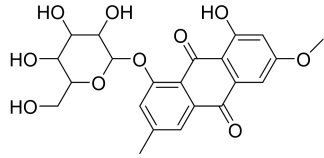
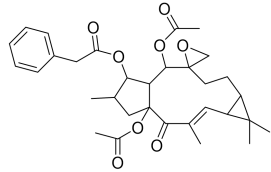
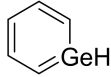
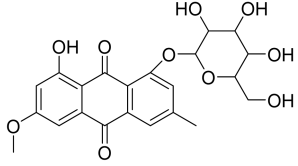
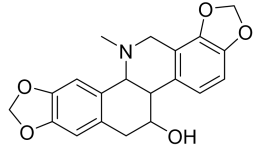
herbs	components	Compound structure
Glycyrrhizae Radix Rhizoma	Glycyrrhizic acid	
	glycyrrhetic acid	
Plumbago zeylanicaL.	Plumbagin	
Aloe、Rhei radix et rhizoma、	Aloe-emodin	
Polygoni Multiflori Radix		
Rhei radix et rhizoma、 Polygoni Multiflori Radix 、 Genkwa Flos 、 Kansui Radix	Emodin	
Artemisiae Argyi Folium 、 Herba	D-camphor	
Asari Forbesii		
Albiziae Cortex	Julibrine II	
Artemisiae Argyi Folium	α -thujone	

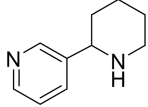
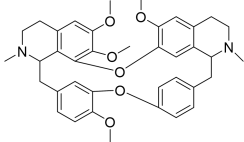
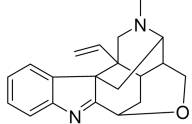
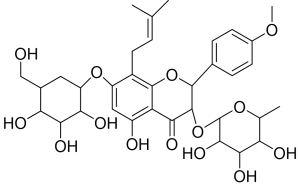
herbs	components	Compound structure
Picrasmae ramulus et folium	4-methoxy-5-hydroxy-canthin-6-one	
Farfarae Flos	Retrorsine	
Castor bean	Ricinine	
Tripterygium Hypoglaucum	Wilforine	
Farfarae Flos Gynura Segetum Senecionis	Senecionine	
Scandentis Hebra Common Threewingnut Root	Celastrol	
Sophorae Tonkinensis Radix et Rhizoma	Sophoranone	
Verbenae Herba	Lycopsamine	
Sinomenii Caulis	Sinomenine	
Komarov Swallowwort	2,2,6,6-tetramethyl-4-piperidone	

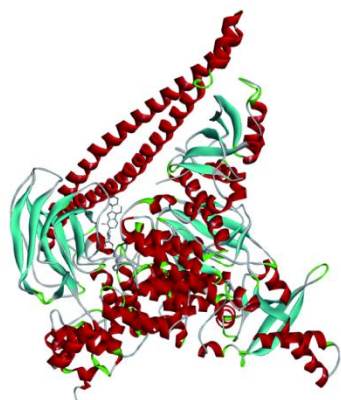
herbs	components	Compound structure
Seeds Of Pachyrhizus Erosus	12 α -hydroxyrotenone	
Aconitum brachypodum Diels	3-acetylaconitine	
Cycas Seed	Cycasin	
Gynura Segetum	Integerrimine	
Tripterygium Hypoglaucomum Common	Triptolide	
Threewingnut Root Rhododendri mollis flos	Rhodojaponin II	
Jatropha curcas	Phorbol ester	
Bulbus Lycoridis Radiatae	Lycorine	
Quisqualis Fructus	Quisqualic acid	
Herba Epimedii	Epimedin C	

herbs	components	Compound structure
Gardeniae Fructus	Geniposide	
Farfarae Flos 、 Senecionis Scandentis Hebra	Senkirkine	
Herba Crotalariae、 Stem and Leaf of Assam Crotalaria	Monocrotaline	
Genkwa Flos	Yuanhuacin	
Frucus Bruceae	Brusatol	
Opium 、 Papaveris Pericarpium	Morphine	
Daturaeflos 、 Physochlainae Radix 、 Datura Seed 、 Folium Daturae Metelis	Scopolamine	
Daturaeflos 、 Physochlainae Radix、 Hyoscyami	Hyoscyamine	
Semen 、 Datura Seed 、 Folium Daturae Metelis	Atropine	

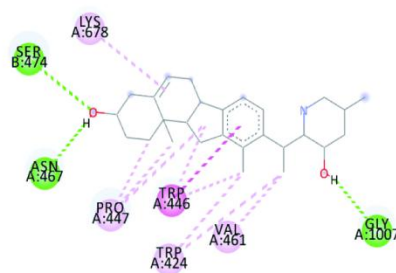
herbs	components	Compound structure
Wooly Datchmanspipe Herb 、 Radix Aristolochiae Cinnabarinae 、 Herba Asari Forbesii 、 Caulis aristolochiae manshuriensis 、 Radix Aristolochiae Fangchi 、 Radix Aristolochiae 、 Aristolo - chia fordiana Hemsl. 、 Fructus Aristolochiae	Aristolochic acid A	
Gynura Segetum、 Senecionis Scandentis Hebra	Seneciophylline	
Aconitum Vilmorinianum Kom. 、 Aconitum brachypodum Diels 、 Aconitum vilmorinianum	Yunaconitine	

herbs	components	Compound structure
Sinopodophyllum hexandrum Dysosma versipellis Sinopodophylli Fructus Radix bupleuri	Podophyllotoxin	
	Saikosaponin A	
	Saikosaponin D	
Fallopia multiflora	Physcion-8-O-β-D-glucopyranoside	
Euphorbia lathyris L.	Euphorbia steroid	
Veratrum viride	Germine	
	Physcion-8-O-glucoside	
Chelidonium majus .L	Chelidoneine	

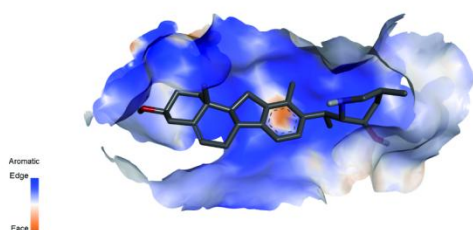
herbs	components	Compound structure
Anabasis aphylla	Anabasine	
Fourstamen Stephania Root	Tetrandrine	
Gelsmium elegans	Koumine	
Icarine	Icariin	



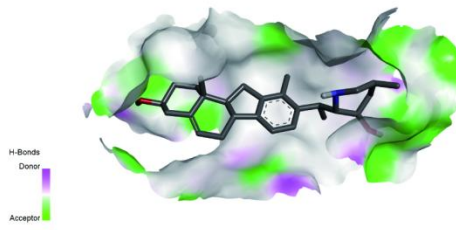
(a) 3D interaction structure of Veratramine with PIK3CA



(b) 2D interaction plane diagram of Veratramine with PIK3CA

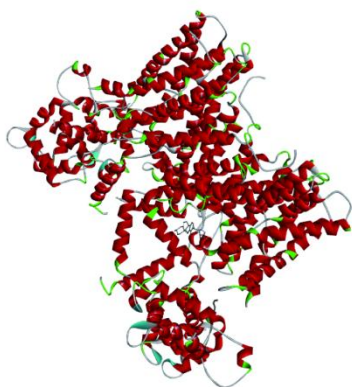


(c) Aromatic interactions between Veratramine and PIK3CA

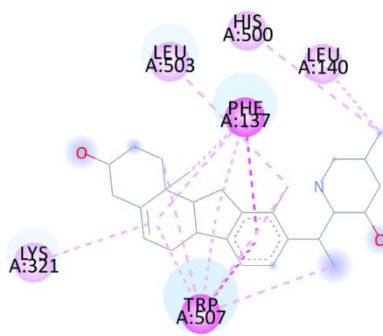


(d) Hydrogen bonding interactions between Veratramine and PIK3CA

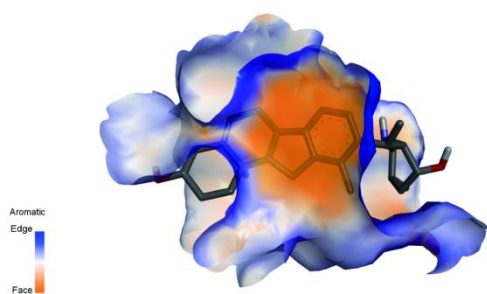
Figure S1. Docking results of Veratramine and PIK3CA molecule. Veratramine was semi-flexibly docked with the protein receptor PIK3CA. From the 2D interaction diagrams, it can be observed that the interacting amino acid residues primarily include ASN467, GLY1007, TRP446, PRO447, TRP424, VAL461, and LYS678. Among them, the oxygen atoms in the Veratramine structure form stable hydrogen bonds with ASN467 and GLY1007. The TRP446 residue engages in Pi-Pi interactions with the benzene ring of Veratramine. Furthermore, the ligand molecule forms Pi-Alkyl interactions with the PRO447, TRP424, and VAL461 residues.



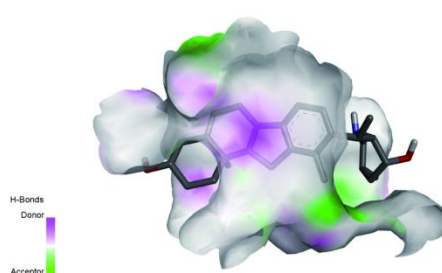
(a) 3D interaction structure of Veratramine with SLC9A3



(b) 2D interaction plane diagram of Veratramine with SLC9A3



(c) Aromatic interactions between Veratramine and SLC9A3

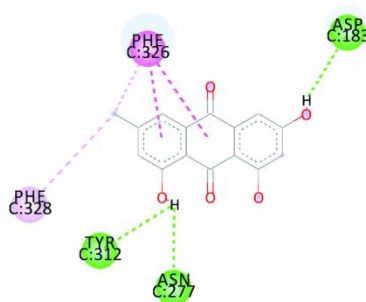


(d) Hydrogen bonding interactions between Veratramine and SLC9A3

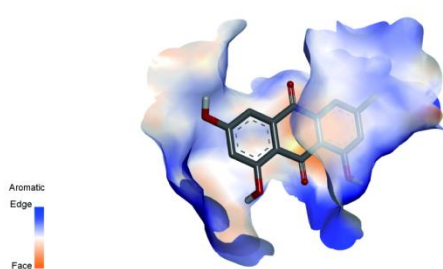
Figure S2. Docking results of Veratramine and SLC9A3 molecule. Veratramine was semi-flexibly docked with the protein receptor SLC9A3. From the 2D interaction diagram, it can be seen that the interacting amino acid residues primarily include TRP507, PHE137, LYS321, LEU140, LEU503, and HIS500. The TRP507 and PHE137 residues engage in Pi-Pi interactions with the benzene ring of Veratramine. Additionally, the ligand molecule forms Pi-Alkyl interactions with the LYS321, LEU140, LEU503, and HIS500 residues.



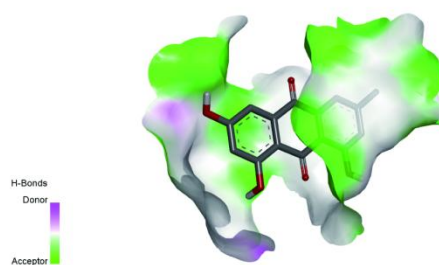
(a) 3D interaction structure of emodin with ACTG2



(b) 2D interaction plane diagram of emodin with ACTG2



(c) Aromatic interactions between emodin and ACTG2

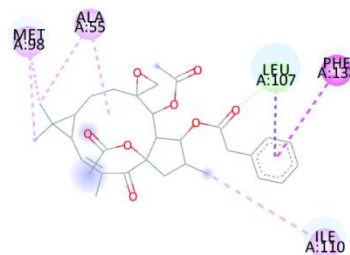


(d) Hydrogen bonding interactions between emodin and ACTG2

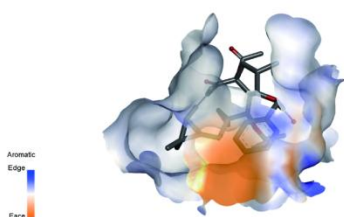
Figure S3. Docking results of emodin and ACTG2 molecule. Emodin was semi-flexibly docked with the protein receptor ACTG2. From the 2D interaction diagram, it can be observed that the interacting amino acid residues primarily include TYR312, ASN277, ASP183, PHE326, and PHE328. The TYR312, ASN277, and ASP183 residues form hydrogen bonds with the hydrogen atoms in the structure of emodin. The PHE326 residue engages in Pi-Pi interactions with the ligand molecule. Additionally, the ligand molecule forms Pi-Alkyl interactions with the PHE328 residue.



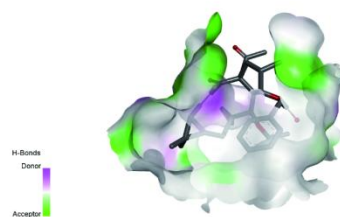
(a) 3D interaction structure of euphobiasteroid with HSP90AA1



(b) 2D interaction plane diagram of euphobiasteroid with HSP90AA1



(c) Aromatic interactions between euphobiasteroid and HSP90AA1



(d) Hydrogen bonding interactions between euphobiasteroid and HSP90AA1

Figure S4. Docking results of euphobiasteroid and HSP90AA1 molecule. Euphobiasteroid was semi-flexibly docked with the protein receptor HSP90AA1. From the 2D interaction diagram, it can be observed that the interacting amino acid residues primarily include LEU107, PHE138, MET98, ALA55, and ILE110. The oxygen atom in the structure of euphobiasteroid forms a stable hydrogen bond with LEU107. The PHE138 residue engages in Pi-Pi interactions with the benzene ring of euphobiasteroid. Additionally, the ligand molecule forms Alkyl interactions with the MET98, ALA55, and ILE110 residues.