Li-Huei Tsai, *et al.*
Enzyme HDAC1 Rejuvenation

https://www.dailymail.co.uk/sciencetech/article-8337373/MIT-researchers-discover-anti-aging-molecule-heal-DNA-lesions-linked-Alzheimers.html

MIT researchers discover 'anti-aging molecule' that can heal DNA lesions linked with Alzheimer's disease and cognitive declines from aging
By Michael Thomsen

Researchers identified the enzyme HDAC1 as helpful in healing DNA damage
As people age, lesions form on parts of their DNA that lowers cognitive function
HDAC1 stimulates production of another enzyme that can heal these lesions

A new joint study from MIT and Harvard has identified an enzyme that could help reverse the effects of DNA damage associated with aging and Alzheimer's disease.

The researchers, led by MIT's Li-Huei Tsai and Harvard's Stephen Haggarty, identified an enzyme called HDAC1 that can help repair 8-oxoguanine lesions on DNA strands, which have been linked to age-related cognitive decline and Alzheimer's.

Test subjects with fewer of these lesions exhibit significantly improved cognitive performance, memory ability and basic spatial awareness.
Researchers identified an enzyme that can heal DNA lesions linked to cognitive decline and Alzheimer's. Scans from mice with an abundance of HDAC1 (top row) had fewer lesions, shown as dark green spots, than mice with no HDAC1 (bottom row)

'It seems that HDAC1 is really an anti-aging molecule,' Tsai told MIT News.

'I think this is a very broadly applicable basic biology finding, because nearly all of the human neurodegenerative diseases only happen during aging. I would speculate that activating HDAC1 is beneficial in many conditions.'

Tsai and Haggerty tested their theory on mice, by genetically engineering some to not produce HDAC1 and comparing them as they aged with a control group with normal levels of HDAC1.

While there were no significant differences initially, over time the mice without the ability to produce HDAC1 developed DNA lesions at a faster rate than for the control and they showed declines in memory tests and spatial navigation.

HDAC1 regulates the production of a separate enzyme, OGG1, which can repair these DNA lesions, but as HDAC1 production decreases with age, so does the brain's ability to heal itself.

The researchers are hopeful that a safe chemical treatment can be found to help stimulate the production for HDAC1 in humans to heal the accumulation of DNA lesions that build up with age

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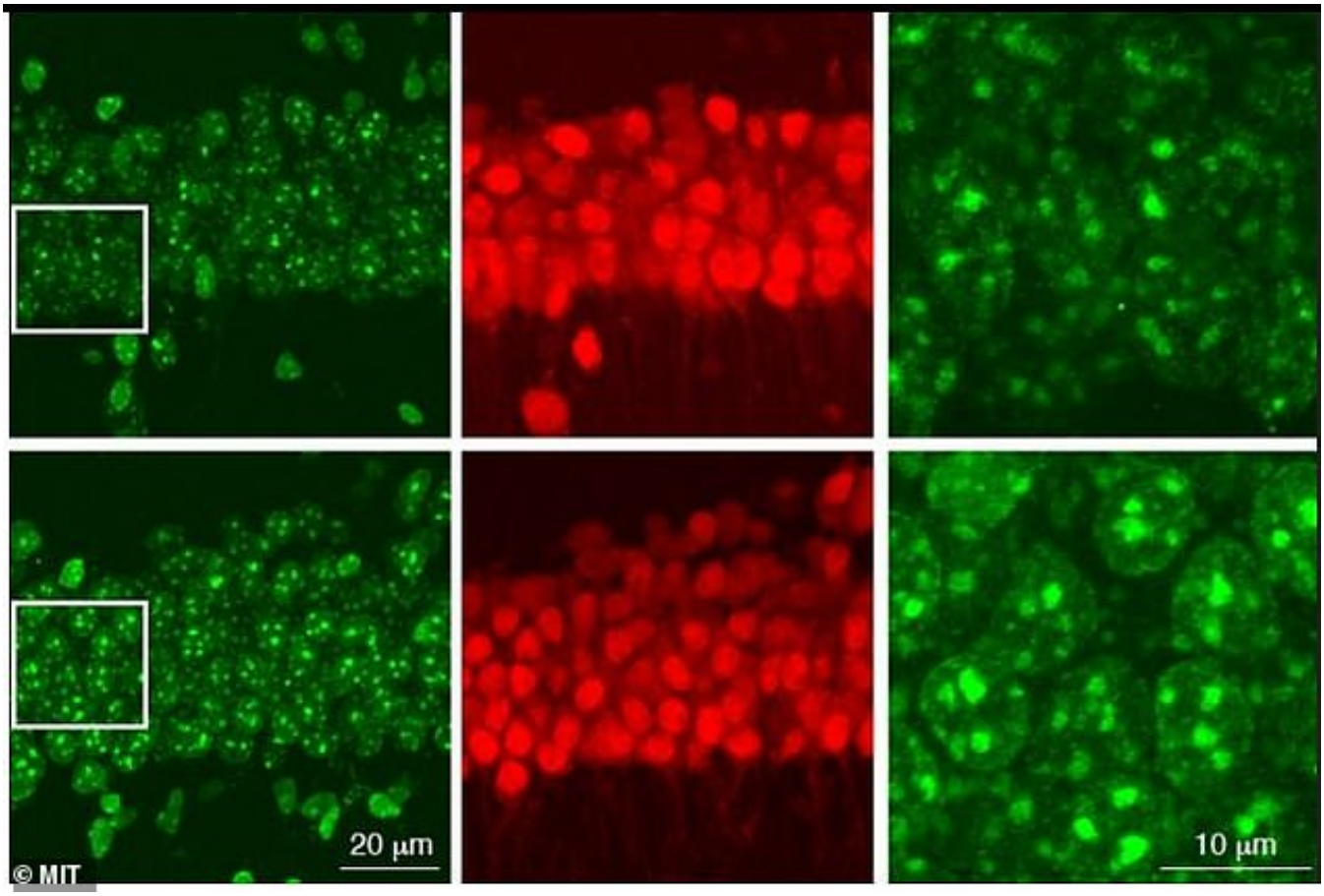
In earlier research, Tsai and her team established that HDAC1 production could be stimulated with the drug exifone, which had been commonly prescribed in the 1980s as a treatment for dementia.

The drug had been discontinued on humans after it was shown to cause liver damage, but in tests on mice, Tsai showed it stimulated the production of HDAC1 and improved the cognitive ability and memory performance in mice.

Tsai also found that the mice had a significant reduction in lesions after being given exifone.

'This study really positions HDAC1 as a potential new drug target for age-related phenotypes, as well as neurodegeneration-associated pathology and phenotypes,' Tsai said.

While the team isn't advocating for exifone to be prescribed to humans, the findings make them hopeful a similar but safer drug could be found to stimulate HDAC1 production as a treatment for cognitive decline and Alzheimer's.



In this figure, neurons in the bottom row, which are missing the HDAC1 gene, show higher levels of DNA damage (green) than normal neurons.

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http://news.mit.edu/2020/aging-neurons-dna-damage-0518
May 18, 2020

Study finds that aging neurons accumulate DNA damage

Reactivating an enzyme that promotes DNA repair can help to reverse age-related cognitive decline in mice.

Anne Trafton

MIT neuroscientists have discovered that an enzyme called HDAC1 is critical for repairing age-related DNA damage to genes involved in memory and other cognitive functions. This enzyme is often diminished in both Alzheimer's patients and normally aging adults.

In a study of mice, the researchers showed that when HDAC1 is lost, a specific type of DNA damage builds up as the mice age. They also showed that they could reverse this damage and improve cognitive function with a drug that activates HDAC1.

The study suggests that restoring HDAC1 could have positive benefits for both Alzheimer's patients and people who suffer from age-related cognitive decline, the researchers say.

"It seems that HDAC1 is really an anti-aging molecule," says Li-Huei Tsai, the director of MIT's Picower Institute for Learning and Memory and the senior author of the study. "I think this is a very broadly applicable basic biology finding, because nearly all of the human neurodegenerative diseases only happen during aging. I would speculate that activating HDAC1 is beneficial in many conditions."

Picower Institute research scientist Ping-Chieh Pao is the lead author of the study, which appears today in Nature Communications.

DNA repair and aging

There are several members of the HDAC family of enzymes, and their primary function is to modify histones — proteins around which DNA is spooled. These modifications control gene expression by blocking genes in certain stretches of DNA from being copied into RNA.

In 2013, Tsai's lab published two papers that linked HDAC1 to DNA repair in neurons. In the current paper, the researchers explored what happens when HDAC1-mediated repair fails to occur. To do that, they engineered mice in which they could knock out HDAC1 specifically in neurons and another type of brain cells called astrocytes.

For the first several months of the mice's lives, there were no discernable differences in their DNA damage levels or behavior, compared to normal mice. However, as the mice aged, differences became more apparent. DNA damage began to accumulate in the HDAC1-deficient mice, and they also lost some of their ability to modulate synaptic plasticity — changes in the strength of the connections between neurons. The older mice lacking HCAC1 also showed impairments in tests of memory and spatial navigation.

The researchers found that HDAC1 loss led to a specific type of DNA damage called 8-oxo-guanine lesions, which are a signature of oxidative DNA damage. Studies of Alzheimer's patients have also shown high levels of this type of DNA damage, which is often caused by accumulation of harmful metabolic byproducts. The brain's ability to clear these byproducts often diminishes with age.

An enzyme called OGG1 is responsible for repairing this type of oxidative DNA damage, and the researchers found that HDAC1 is needed to activate OGG1. When HDAC1 is missing, OGG1 fails to turn on and DNA damage goes unrepaired. Many of the genes that the researchers found to be most susceptible to this type of damage encode ion channels, which are critical for the function of synapses.

Targeting neurodegeneration

Several years ago, Tsai and Stephen Haggarty of Harvard Medical School, who is also an author of the new study, screened libraries of small molecules in search of potential drug compounds that activate or inhibit members of the HDAC family. In the new paper, Tsai and Pao used one of these drugs, called exifone, to see if they could reverse the age-related DNA damage they saw in mice lacking HDAC1.

The researchers used exifone to treat two different mouse models of Alzheimer's, as well as healthy older mice. In all cases, they found that the drug reduced the levels of oxidative DNA damage in the brain and improved the mice's cognitive functions, including memory.

Exifone was approved in the 1980s in Europe to treat dementia but was later taken off the market because it caused liver damage in some patients. Tsai says she is optimistic that other, safer HDAC1-activating drugs could be worth pursuing as potential treatments for both age-related cognitive decline and Alzheimer's disease.

"This study really positions HDAC1 as a potential new drug target for age-related phenotypes, as well as neurodegeneration-associated pathology and phenotypes," she says.

Tsai's lab is now exploring whether DNA damage and HDAC1 also play a role in the formation of Tau tangles — misfolded proteins in the brain that are a signature of Alzheimer's and other neurodegenerative diseases.

The research was funded by the National Institute on Aging, the National Institute of Neurological Disorders and Stroke, and a Glenn Award for Research in Biological Mechanisms of Aging.

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https://www.sciencedirect.com/science/article/abs/pii/S0165614710001665
Trends in Pharmacological Sciences, Volume 31, Issue 12, December 2010, Pages 605-617
https://doi.org/10.1016/j.tips.2010.09.003

Targeting the correct HDAC(s) to treat cognitive disorders
A. Fischer, et al.

Changes in gene expression in the brain may underlie cognitive deficits inherent to normal aging and neurodegenerative disease. However, the mechanisms underlying pathological alterations in the brain transcriptome are incompletely understood. Epigenetic mechanisms such as DNA methylation and histone acetylation have been shown to be important for memory processes in the adult brain. There is accumulating evidence that altered chromatin plasticity and histone acetylation are also involved in cognitive aging, neurodegeneration, and neuropsychiatric diseases. Inhibitors of histone deacetylase (HDAC) exhibit neuroprotective and neuroregenerative properties in animal models of various brain diseases. As such, targeting of HDACs seems to be a promising therapeutic strategy. In this review, we discuss the specific roles of each HDAC protein and the possible function of distinct histone modifications. We hope that this knowledge will aid in the development of diagnostic tools and in designing more potent and specific treatment for neurological disorders targeting selective HDAC proteins.

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https://www.sciencedirect.com/science/article/pii/S089662730800888X
Neuron, Volume 60, Issue 5, 10 December 2008, Pages 803-817

https://doi.org/10.1016/j.neuron.2008.10.015

Deregulation of HDAC1 by p25/Cdk5 in Neurotoxicity
Dohoon Kim, et al.

Summary
Aberrant cell-cycle activity and DNA damage are emerging as important pathological components in various neurodegenerative conditions. However, their underlying mechanisms are poorly understood. Here, we show that deregulation of histone deacetylase 1 (HDAC1) activity by p25/Cdk5 induces aberrant cell-cycle activity and double-strand DNA breaks leading to neurotoxicity. In a transgenic model for neurodegeneration, p25/Cdk5 activity elicited cell-cycle activity and double-strand DNA breaks that preceded neuronal death. Inhibition of HDAC1 activity by p25/Cdk5 was identified as an underlying mechanism for these events, and HDAC1 gain of function provided potent protection against DNA damage and neurotoxicity in cultured neurons and an in vivo model for ischemia. Our findings outline a pathological signaling pathway illustrating the importance of maintaining HDAC1 activity in the adult neuron. This pathway constitutes a molecular link between aberrant cell-cycle activity and DNA damage and is a potential target for therapeutics against diseases and conditions involving neuronal death.

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https://www.annualreviews.org/doi/abs/10.1146/annurev-pharmtox-011112-140216
Annual Review of Pharmacology and Toxicology
Vol. 53:311-330 (January 2013)
https://doi.org/10.1146/annurev-pharmtox-011112-140216

The Potential of HDAC Inhibitors as Cognitive Enhancers
Johannes Gräff and Li-Huei Tsai

Abstract
Histone acetylation is a prominent epigenetic modification of the central nervous system that is unequivocally associated with an increase in the rate of gene transcription. Because gene transcription, in turn, plays an important role in long-lasting forms of memory, histone acetylation generally favors long-term memory, whereas histone deacetylation impinges on it. Histone acetylation is also amenable to pharmacological interventions—predominantly by the use of histone deacetylase (HDAC) inhibitors—and has therefore spurred considerable interest as a putative target of cognitive enhancement. Because of the ubiquitous presence of histone acetylation, HDAC inhibitors have great potential not only to treat cognitive impairment resulting from neurodevelopmental and neurodegenerative disorders but also to serve as cognitive enhancers for the cognitively healthy. In this review, we summarize the state of the art of HDAC inhibitors as cognitive treatments or cognitive enhancers; describe a new model of their mode of action, epigenetic priming; and caution against their unsupervised usage, despite their overall great promise.

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https://www.nature.com/articles/nn.3514
Nature Neuroscience volume 16, pages1383–1391(2013)

Interaction of FUS and HDAC1 regulates DNA damage response and repair in neurons
Wen-Yuan Wang, et al.

Abstract

Defects in DNA repair have been extensively linked to neurodegenerative diseases, but the exact mechanisms remain poorly understood. We found that FUS, an RNA/DNA-binding protein that has been linked to amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration, is important for the DNA damage response (DDR). The function of FUS in DDR involved a direct interaction with histone deacetylase 1 (HDAC1), and the recruitment of FUS to double-stranded break sites was important for proper DDR signaling. Notably, FUS proteins carrying familial ALS mutations were defective in DDR and DNA repair and showed a diminished interaction with HDAC1. Moreover, we observed increased DNA damage in human ALS patients harboring FUS mutations. Our findings suggest that an impaired DDR and DNA repair may contribute to the pathogenesis of neurodegenerative diseases linked to FUS mutations.

US20100075926
Activation of histone deacetylase 1 (hdac1) protects against dna damage and increases neuronal survival
[PDF]

Abstract
The invention provides methods and compounds for the treatment of neurological disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS (Amyotrophic Lateral Sclerosis), traumatic brain injury, ischemic brain injury or a stroke. In one aspect the compounds are HDAC1 activators. Exemplary HDAC1 activators include metal chelators, iron chelators, deferoxamin, flavonoids, compounds comprising a catechol moity, ginkgetin K, Chembridge 5104434, sciadopilysin, tetrahydrogamboic acid, TAM-11, LY 235959, CGS 19755, SK&F 97541, etidronic acid, levonordefrin, methyldopa, ampicillin trihydrate, D-aspartic acid, gamma-D-glutamylaminomethylsulfonic acid, phenazopyridine to hydrochloride, oxalamine citrate salt, podophyllotoxin, SK&F 97541, (+-)-4-amino-3-(5-chloro-2-thienyl)-butanoic acid, (RS)-(tetrazol-5-yl) glycine, R(+)-SKF-81297, gambogic acid, and derivatives thereof.

Other Enzyme HDAC1 Patents

KR20150132342
HISTONE DEACETYLASE INHIBITORS
[PDF]

Abstract
A histone deacetylase ("HDAC") enzyme (for example, HDAC1, HDAC2, and HDAC3) the compounds and methods for inhibiting is provided herein.

KR20150132345
HDAC INHIBITORS
[PDF]

Abstract
Compounds and deacetylase ("HDAC") enzyme histone using a compound of formula (I) of formula (I) a method for inhibiting (for example, HDAC1, HDAC2, and HDAC3) are disclosed herein:

CN106177019

HDAC1 enzyme inhibiting effective fraction of comarum salesovianum, preparation method and applciation

[PDF]

Abstract

The invention discloses an HDAC1 enzyme inhibiting effective fraction of comarum salesovianum, a preparation method and application, and belongs to the technical field of plant extracts. The HDAC1 enzyme inhibiting effective fraction of the comarum salesovianum is selected from one of an n-butanol fraction of the comarum salesovianum and an aqueous-phase extraction fraction of the comarum salesovianum or is a mixture of the n-butanol fraction of the comarum salesovianum and the aqueous-phase extraction fraction of the comarum salesovianum in any mass ratios. The comarum salesovianum is crushed, an ethanol solution with the volume percentage concentration of 65% to 95% is added for reflux extraction, an obtained extracting solution is concentrated and dried to obtain extract, the extract is dispersed by adding distilled water to obtain extract dispersing liquid, the extract dispersing liquid is extracted by taking petroleum ether, ethyl acetate and n-butyl alcohol as solvents sequentially, and after the solvents are removed through volatilization, the n-butanol fraction of the comarum salesovianum is obtained; the remaining extract dispersing liquid obtained after extraction is concentrated and dried, and the aqueous-phase extraction fraction of the comarum salesovianum is obtained. Application of the HDAC1 enzyme inhibiting effective fraction of the comarum salesovianum in preparation of HDAC1 enzyme inhibiting drugs is achieved, and the HDAC1 enzyme inhibiting effective fraction can be used for preparing anti-tumor drugs.

CN108003111

Double-target-point inhibitor based on HDAC1 and IDO1 and preparation method and application thereof

[PDF]

Abstract

The invention discloses a double-target-point inhibitor based on HDAC1 and IDO1 and a preparation method and application thereof. The structure of the inhibitor is shown in the general formula A. Thedefinitions of all substituent groups are shown in the description and the patent claim. It is proved through pharmacological experiments that a compound has good HDAC1 and IDO1 enzyme inhibition activity and has in-vitro antitumor activity with a certain broad spectrum. It is proved through in-vivo experiments that the compound can effectively lower in-vivo IDO1 activity and remarkably delay thetumor growth and can be applied to tumor diseases of pathological characteristics of an IDO1-mediated tryptophan metabolic pathway. The compound is used as reported double-target-point antitumor medicine based on HDAC1 and IDO1 for the first time and has the further development and research values.

US2009298046

Assays for Histone Deacetylase 1/2 Selective Inhibitors

Abstract

The present invention relates to an assay specific for histone deacetylases HDAC1 and/or 2 inhibitors which comprises: (i) incubating an HDAC1 and/or 2 enzymes(s) together with a protein that contains the SANT and ELM2 regions, found in MTA proteins such as MTA-2, MTA-1, MTA-3 and also found in CoREST, CoREST2, CoREST3 and MI-ER1, in a suitable assay buffer (ii) adding the potential HDAC inhibitor and a suitable substrate and incubating (iii) stopping the

incubation and determining the effect the putative HDAC inhibitor has had on enzyme activity by comparison with standards.

CN106236842

Tinospora sinensis HDAC1 enzyme inhibition effective part, as well as preparation method and application thereof

[PDF]

Abstract

The invention discloses a tinospora sinensis HDAC1 enzyme inhibition effective part, as well as a preparation method and application thereof, and belongs to the technical field of plant extracts. The corydalis pygmaea effective part is one of a corydalis pygmaea petroleum ether part and a corydalis pygmaea aqueous extraction part, or a mixture of more than two of a corydalis pygmaea petroleum ether part, a corydalis pygmaea ethyl acetate part, a corydalis pygmaea n-butyl alcohol part and a corydalis pygmaea aqueous extraction part in an arbitrary mass ratio. The preparation method comprises the following steps of: grinding corydalis pygmaea, refluxing and extracting with an ethanol solution having a volume percentage concentration of 65-95 percent, concentrating and drying the extract to obtain an extract; dispersing the extract with distilled water to obtain an extract dispersant, extracting the extract dispersant sequentially with petroleum ether, ethyl acetate and n-butyl alcohol, and volatilizing a solvent to obtain a corydalis pygmaea petroleum ether part, a corydalis pygmaea ethyl acetate part and a corydalis pygmaea n-butyl alcohol part; and concentrating and drying the extracted extract dispersant to obtain a corydalis pygmaea water-phase extraction part. The corydalis pygmaea HDAC1 enzyme inhibition effective part can be applied to preparation of medicines for inhibiting HDAC1 enzyme, and can be used for preparing anti-tumor medicines.

CN106333969

Agaricus gennadii HDAC1 enzyme inhibition effective part and preparation method and application

[PDF]

Abstract

The invention provides an agaricus gennadii HDAC1 enzyme inhibition effective part and a preparation method and application and belongs to the technical field of plant extracts. The effective part is selected from a mixture of one or more of an agaricus gennadii petroleum ether part, an agaricus gennadii ethyl acetate part, an agaricus gennadii n-butyl alcohol part and an agaricus gennadii aqueous phase extraction part according to any mass ratio. Agaricus gennadii is smashed, an ethyl alcohol solution with the volume percentage concentration being 65-95% is added for reflux extraction, and an obtained extracting solution is concentrated and dried to obtain an extract; the extract is added into distilled water to be dispersed, an extract dispersion solution is obtained and extracted by sequentially using petroleum ether, ethyl acetate and n-butyl alcohol as solvents, and the agaricus gennadii petroleum ether part, the agaricus gennadii ethyl acetate part and the agaricus gennadii n-butyl alcohol part are obtained after the solvents are removed through volatilization; the remaining extract dispersion solution obtained after extraction is concentrated and dried, and the agaricus gennadii aqueous phase extraction part is obtained. The agaricus gennadii HDAC1 enzyme inhibition effective part is applied to preparing HDAC1 enzyme inhibition medicine and can be used for preparing anti-tumor medicine.

CN106176843

Effective epilobium angustifolium L. part for restraining HDAC1 enzyme and preparation method and application

[PDF]

Abstract

The invention discloses an effective epilobium angustifolium L. part for restraining HDAC1 enzyme and a preparation method and application and belongs to the technical field of plant extractive. The effective epilobium angustifolium L. part is a mixture obtained by selecting one or more of epilobium angustifolium L. ethyl acetate extract, epilobium angustifolium L. n-butyl alcohol extract and epilobium angustifolium L. water-phase extract according to any mass ratio. Whole grass of epilobium angustifolium L. is smashed and added into ethanol water with the volume percent concentration being 65-95% to be subjected to reflux extraction, an obtained extracting solution is concentrated and dried, and extract is obtained; distilled water is added into the extract for dispersion, extract dispersion liquid is obtained, petroleum ether, ethyl acetate and ethyl acetate sequentially serve as solvents to extract the extract dispersion liquid, and after the solvents are volatized, the epilobium angustifolium L. ethyl acetate extract and the epilobium angustifolium L. n-butyl alcohol extract are obtained; the extracted extract dispersion liquid is concentrated and dried, and the epilobium angustifolium L. water-phase extract is obtained. The effective epilobium angustifolium L. part for restraining the HDAC1 enzyme is applied to preparation of medicines for restraining the HDAC1 enzyme and can be used for preparing antitumor medicines.

WO2015149435

E-CONFIGURATION BENZAMIDE COMPOUND AND PHARMACEUTICAL FORMULATION AND APPLICATION THEREOF

[PDF]

Abstract

Disclosed are an E-configuration benzamide compound and pharmaceutical formulation and application thereof. The E-configuration benzamide compound has a structure represented by formula (I), with the chemical name of N-(2-amino-4-fluorophenyl)-4-[N-[(E)-3-(3-pyridine) acryl] aminomethyl] benzamide, and 3-pyridine acryl in the structural formula having E-configuration. The E-configuration benzamide compound represented by formula (I) has subtype selective histone deacetylated enzyme inhibitory activity, mainly inhibiting HDAC1, HDAC2, HDAC3 in type I HADC and HDAC10 in type IIb HDAC. The E-configuration benzamide compound represented by formula (I) can be used to treat diseases related to abnormal activity of the histone deacetylated enzyme, such as cancer, including lymphoma, solid tumor and blood system tumor and the like.

CN106344660

Effective parts of corydalis impatiens and preparing method and application thereof

[PDF]

Abstract

Effective parts of corydalis impatiens and preparing method and application thereof belong to the field of plant extract technology, which is selected from the total alkaloid extract of corydalis impatiens. The herb is smashed and added into a ethanol solution with the mass percentage of 65% - 95% for reflux extraction. And the yielded extract solution is concentrated and dried to obtain the extract, in which a hydrochloric acid aqueous solution is added with a mass concentration of 2%. After removal of the fat-soluble impurities, the pH is adjusted to 9 to 10 by adding some ammonium hydroxide. Finally, the extract is obtained by multiple extractions with chloroform, and is concentrated and dried to obtain the total alkaloid extract of corydalis impatiens. The effective part of corydalis impatiens in this invention can be used for preparing anti-tumor drugs, for the

application of the effective part of corydalis impatiens in the preparation of drugs for inhibiting HDAC1 enzyme.

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http://www.efloras.org/florataxon.aspx?flora_id=2&taxon_id=200009130
Corydalis impatiens (Pallas) Fischer in Candolle, Syst. Nat. 2: 124. 1821.

Corydalis impatiens

Fumaria impatiens Pallas, Reise Russ. Reich. 3: 286. 1776; Corydalis impatiens var. minima Michajlova; C. sibirica (Linnaeus f.) Persoon subsp. impatiens (Pallas) A. Gubanov; C. sibirica var. impatiens (Pallas) Regel.

Herbs, annual or more often ?biennial, 10-40 cm tall, glabrous, with taproot. Stems erect to suberect, often purplish, winged-ridged, branched from base and above. Petiole of basal leaves 4-6 cm, vaginate at base; blade glaucous abaxially, green or glaucous adaxially, bi- to triternate; leaflets deeply divided into 2 or 3 obovate to oblanceolate, obtuse to subacute mucronate lobes. Racemes 5-11-flowered, rather lax in fruit; lowermost bract often large and divided, middle and upper bracts usually entire, lanceolate, 5-7 mm. Pedicel 3-5 mm, recurved in fruit. Sepals minute, ca. 0.5 mm, dentate. Corolla pale yellow; outer petals obtuse, mucronate, with narrow usually dentate crests slightly overtopping apex; spur of upper petal 2-3 mm, obtuse; nectary ca. 1/2 as long as spur; lower petal without basal pouch; inner petals 4-5 mm. Stigma with narrow sinus, 4 apical stalked papillae, and a pair of geminate papillae close to apex. Fruit oblong, 9-14 × ca. 2 mm, 3-8-seeded; style short, 1(-1.5) mm. Seeds in 1 row, 1.6-1.7 mm, smooth; elaiosome small. Fl. and fr. Jun-Oct.

Forest understories, shrubs on slopes, tussocks, roadsides; ca. 1700 m. N Gansu, Jilin, Nei Mongol (Wulashan), N Qinghai, Shanxi (Dawutai Shan) [Mongolia, Russia (Siberia)].

CN106176984
Effective part of Corydalis conspersa as well as preparation method and application of effective part
[PDF]

Abstract
The invention provides an effective part of Corydalis conspersa as well as a preparation method and an application of the effective part and belongs to the technical field of plant extracts. The effective part of the Corydalis conspersa is selected from one of an ethyl acetate extract of the Corydalis conspersa, an n-butyl alcohol extract of the Corydalis conspersa and an aqueous extraction extract of the Corydalis conspersa or a mixture of two or more of the extracts of the Corydalis conspersa in any mass ratio. The preparation method comprises steps as follows: the herb of the Corydalis conspersa is ground, an ethanol solution with volume percentage concentration being 65%-95% is added for reflux extraction, an obtained extracting solution is concentrated and dried, and extractum is obtained; distilled water is added to the extractum, the extractum is dispersed, an extractum dispersion liquid is obtained and is extracted with petroleum ether, ethyl acetate and n-butyl alcohol as solvents sequentially, and after solvents are volatilized, the ethyl acetate extract of the Corydalis conspersa and the n-butyl alcohol extract of the Corydalis conspersa are obtained; the extractum dispersion liquid after extraction is concentrated and dried, and the aqueous extraction extract of the Corydalis conspersa is obtained. According to the application of the effective part of the Corydalis conspersa in preparation of drugs for inhibiting CDC25 enzyme and HDAC1 enzyme, the effective part of the Corydalis conspersa can be used for preparing antitumor drugs.

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https://species.wikimedia.org/wiki/Corydalis_conspersa

Corydalis conspersa

Familia: Papaveraceae
Subfamilia: Fumarioideae
Tribus: Fumarieae
Genus: Corydalis
Species: Corydalis conspersa

CN106344668
Effective parts of skyblue adonis and preparation method and application thereof
[PDF]

Abstract
The invention discloses the effective parts of skyblue adonis and the preparation method and application thereof and belongs to the technical field of plant extract. The method comprises of the steps of selecting the mixture of one or more than two extracts from the petroleum ether part, ethyl acetate, normal butyl alcohol part and water phase extraction part of skyblue adonis. Crushing the skyblue adonis and adding 65%-95% (weight) ethanol solution for extraction, concentrating and drying the extracting solution to obtain the extract; adding distilled water for dispersion to obtain extract dispersion, then respectively using petroleum ether, ethyl acetate and normal butyl alcohol as the solvent to extract the extract dispersion, making the solvent volatilize to obtain the petroleum ether part, ethyl acetate, normal butyl alcohol part and water phase extraction part of skyblue adonis; concentrating and drying the extracted extract dispersion to obtain the water phase extraction part of skyblue adonis. The effective parts of skyblue adonis of the invention can be used to prepare drugs inhibiting HDAC1 enzyme, and prepare cancer resistant drugs.

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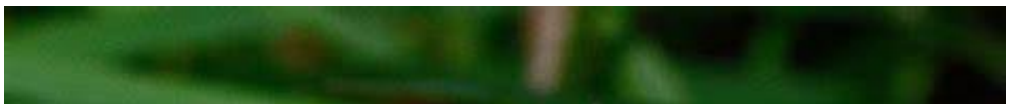
https://butterfly-conservation.org/butterflies/adonis-blue

Adonis Blue



The Adonis Blue overwinters as a caterpillar; it is is green with short, yellow stripes, which camouflage it while it feeds on Horseshoe Vetch during the day. It is most commonly seen during April and late July as it searches for ants to 'milk' its sugary secretions.

https://en.wikipedia.org/wiki/Polyommatus_bellargus
The Adonis blue (Lysandra bellargus, also known as Polyommatus bellargus) is a butterfly in the family Lycaenidae. It is found in the Palearctic ecozone (Western Europe, Central Europe, South Europe, South Russia, Iraq, Iran, Caucasus, Transcaucasus, Turkey).
It is found in chalk downland, in warm sheltered spots, flying low over vegetation, seeking females that are rich chocolate brown in color. The male has brilliantly colored wings that give it its name.

CN106236809
Saussurea-obvallata effective part and preparing method and application thereof
[PDF]

Abstract
The invention discloses a saussurea-obvallata effective part and a preparing method and application thereof, and belongs to the technical field of plant extract. The saussurea-obvallata effective part is selected from the mixture of any mass ratio of one or two above of a saussurea-obvallata petroleum ether part, a saussurea-obvallata ethyl acetate part, a saussurea-obvallata n-butyl alcohol part and a saussurea-obvallata aqueous phase extraction part. The preparing method includes the steps that saussurea-obvallata whole plant is smashed, an ethanol solution with the mass percent concentration of 65% to 95% is added and subjected to reflux extraction, the obtained extracted liquid is concentrated and dried, and extract is obtained; the extract is dispersed in distilled water, extract dispersion liquid is obtained, petroleum ether, ethyl acetate and n-butyl alcohol are sequentially used as a solvent to extract the extract dispersion liquid, and after the solvent is volatilized, the saussurea-obvallata petroleum ether part, the saussurea-obvallata ethyl acetate part and the saussurea-obvallata n-butyl alcohol part are obtained; the extracted extract dispersion liquid is concentrated and dried, and the saussurea-obvallata aqueous phase extraction part is obtained. The saussurea-obvallata effective part has an application to preparing medicine for inhibiting a

HDAC1 enzyme, and can be used for preparing antitumor medicine.

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https://en.wikipedia.org/wiki/Saussurea_obvallata

Saussurea obvallata

Saussurea obvallata is a species of flowering plant in the Asteraceae. It is native to the Himalayas, Himachal Pradesh and Uttarakhand, India, Mongolian, northern Burma and southwest China. In the Himalayas, it is found at an altitude of around 4500 m.

CN106236853

Corydalis pygmaea effective part, as well as preparation method and application thereof

[PDF]

Abstract

The invention discloses a corydalis pygmaea effective part, as well as a preparation method and application thereof, and belongs to the technical field of a plant extract. The corydalis pygmaea effective part is mixture of one or more than one of a corydalis pygmaea petroleum ether part, a corydalis pygmaea ethyl acetate part and a corydalis pygmaea aqueous extraction part in an arbitrary mass ratio. The preparation method comprises the following steps: grinding whole grass of corydalis pygmaea, refluxing and extracting with an ethanol solution having a volume percentage concentration of 65-95 percent, concentrating and drying the extract to obtain an extract; dispersing the extract with distilled water to obtain an extract dispersant, extracting the extract dispersant sequentially with petroleum ether, ethyl acetate and n-butyl alcohol, and volatizing solvent to obtain a corydalis pygmaea petroleum ether part and a corydalis pygmaea ethyl acetate part; and concentrating and drying the extracted extract dispersant to obtain a corydalis pygmaea water-phase extraction part. The corydalis pygmaea effective part can be applied to preparation of medicines for inhibiting HDAC1 enzyme, and can be used for preparing anti-tumor medicines.

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Corydalis pygmaea C. Y. Wu & Z. Y. Su, Acta Bot. Yunnan. 2: 208. 1980.

Corydalis pygmaea 矮黄堇 ai huang jin

CN106236829

Dracocephalum tanguticum maxim effective part as well as preparation method and application thereof

[PDF]

Abstract

The invention discloses a dracocephalum tanguticum maxim effective part as well as a preparation method and an application thereof, and belongs to the technical field of plant extracts. The dracocephalum tanguticum maxim effective part is selected from any one or any mixtures at any mass ratios of the follows: a dracocephalum tanguticum maxim ethyl acetate extract, a dracocephalum tanguticum maxim n-butanol extract and a dracocephalum tanguticum maxim aqueous extract. The dracocephalum tanguticum maxim ethyl acetate extract, the dracocephalum tanguticum maxim n-butanol extract and the dracocephalum tanguticum maxim aqueous extract are prepared by the following steps: crushing whole herb of dracocephalum tanguticum maxim,

conducting reflux extraction with the addition of an ethanol solution which is 65-95% in mass percentage concentration, and concentrating and drying an obtained extracting solution, so that an extractum is obtained; dispersing the extractum with the addition of distilled water, so that extractum dispersion liquid is obtained; extracting the extractum dispersion liquid by taking petroleum ether, ethyl acetate and n-butanol as solvents sequentially, and conducting volatilizing and removing the solvents, so as to obtain the dracocephalum tanguticum maxim ethyl acetate extract and the dracocephalum tanguticum maxim n-butanol extract; and concentrating and drying the extracted extractum dispersion liquid, so that the dracocephalum tanguticum maxim aqueous extract is obtained. The dracocephalum tanguticum maxim effective part disclosed by the invention is applicable to the aspect of preparing drugs for inhibiting HDAC1 enzyme; and the dracocephalum tanguticum maxim effective part can be used for preparing anti-tumors drugs.

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Dracocephalum tanguticum Maximowicz, Bull. Acad. Imp. Sci. Saint-Pétersbourg. ser. 3, 27:530. 1881.

Dracocephalum tanguticum

Click to enlarge **Credit: Harvard University Herbaria**

Herbs perennial, fetid. Stems erect, to 55 cm, obtusely 4-angled, retrorse pubescent toward apex, subglabrous basally, internodes 2.5-6 cm. Petiole 3-8 mm; leaf blade pinnatisect, elliptic-ovate to elliptic, 2.6-4(-7.5) × 1.4-2.5(-4.2) cm, base broadly cuneate, adaxially glabrous, abaxially glabrous to densely gray pubescent; segments in 2 or 3 pairs, linear, 0.7-1.9(-3) cm × 1-2(-3) mm, ter-minal section 1.4-2.8(-4.4) cm, margin entire, involute. Verticillasters 2-6-flowered, in 5-9 upper stem nodes; floral leaves similar to cauline leaves but much reduced, with 1 pair of segments, 5-7 mm, pubescent, ciliate. Calyx purplish, 1-1.4 cm, densely spreading pubescent, golden glandular, split to 1/3 its length; teeth margin ciliate, apex acute; upper lip teeth broadly lanceolate, middle tooth subequal to lateral lobes, lower lip teeth lanceolate. Corolla purple-blue to dark purple, 2-2.7 cm, pubescent, lower lip 2 × as long as upper lip. Fl. Jun-Sep.

* Riverbanks, fields, grassy beaches, dry lake beds, sunny hillsides, pine forest margins; 3200-4700 m. Gansu, Qinghai, Sichuan, Xizang

1 Stems unbranched; leaves abaxially glabrous 4b var. nanum

+ Stems branched along entire length; leaves abaxially densely hairy. (2)

2 (1) Stems 35-55 cm; leaves abaxially gray pubescent 4a var. tanguticum

+ Stems less than 35 cm; leaves abaxially gray tomentulose 4c var. cinereum