

black pepper / white pepper

black pepper is the dried, fullgrown but unripe fruit of the perenial woody vine *piper nigrum l*, while white pepper is obtained from the dried ripe fruit by removing the outer portion of the pericarp after soaking in water [01]

black pepper is the dried, unripe fruit of the tropical plant, *piper nigrum l*, and contains about 5-10% piperine ... , 1-2,5% essential oils ... [21]

black pepper contains on average 12,5% water, white pepper 13,5%

	anhydrous pepper	
	<i>black</i>	<i>white</i>
	average content in %	
piperine	7.5	7.8
piperidine	0.6	0.3
nitrogen containing substance	12.8	11.9
essential oil	2.25	1.5
ether extract	9.1	8
alcohol extract	10.3	9.1
starch	36.5	56.8
cellulose	14	4.4
resin	1.05	0.35
ash	5.15	1.9

[roempp, entry pfeffer]

oil of pepper [merck index]

PEPPER ANALYSIS - A Critical Study of Two Procedures for the Determination of Piperine in Black and White Pepper [02]

piper [kad]

long pepper

long pepper contains the alkaloid piperine (about 6%), which is slightly higher than that in black pepper. [25]

... we performed a quantitative determination of piperine in three different pepper species ... black, white and green pepper.

we used HPLC with a 70% methanol-30%water eluent. the results are as follows:

<i>pepper</i>	<i>piperine</i>
black	2.0%
white	2.4%
green	3.8%

[22]

piperine occurrence

botanical name	common name	piperine	reference
<i>piper nigrum</i>	white pepper	7.8%	[roempp, entry pfeffer]
	black pepper	7.5%	
		6-9%	[04]
		9.2%	[23]
		5-10%	[21]
	11%	[04, (15)]	
<i>piper longum</i> <i>piper retrofractum</i>	long pepper (green pepper)	6% 5%	[25] [04]
<i>piper clusii</i>	ashanti pepper	5%	[04, (12,13)]
<i>piper lowong</i>		1.5%	[04, (13)]
<i>piper famechoni</i>			[06, page 233-236, (3)]
<i>piper chaba</i>			[06, page 233-236, (4)]

further references

references: [pepper](#)

references

[merck index]

THE MERCK INDEX on CD-ROM / Version 12:3 / 1999

[roempp]

roempp lexikon chemie version 2.0, cd-rom,
stuttgart / new york: georg thieme verlag 1999

[kad]

[king's american dispensatory](#) 1898

m d harvey wickes felter, phr m ph d john uri lloyd

[01]

journal of chemical education 1993 70(7): 598-599

"isolation of piperine from black pepper"

william w epstein, david f netz, jimy l seidel

[02]

[j agric food chem 1963 11\(6\): 508-512](#)

"PEPPER ANALYSIS - A Critical Study of Two Procedures for the Determination of Piperine in Black and White Pepper"
CHRISTIANE GENEST, D MORISON SMITH, D G CHAPMAN

[04]

leo marion, II. the pepper alkaloides, 1. piperine, p.168,
the alkaloids, chemistry and physiology, volume I,
academic press inc, publishers, new york, 1950

[06]

"**natural products - a laboratory guide**", 1991 2.edition
raphael ikan; academic press, inc; ISBN 0-12-370551-7

[21]

patent [US4820517](#), 1989-04-11

"**process for obtaining a pepper extract with insecticidal activity**"

HANS PFEIFFER, MANFRED BIERMANN, PETER SCHROEDER,
GERD GOEBEL, ANNEMARIE MUELLER; HENKEL KGAA

abstract: PCT No. PCT/EP85/00333 Sec. 371 Date Jul. 24, 1986 Sec. 102(e) Date Jul. 24, 1986 PCT Filed Jul. 6, 1985 PCT Pub. No. WO86/01981 PCT Pub. Date Apr. 10, 1986. An insecticidally active fraction is obtained from black pepper by a process comprising the following steps: (a) extraction of black pepper in ground form with CO₂ at 30 to 70°C and 150 to 500 bar; (b) removal of sharp tasting fractions therein in a first expansion step at 25 to 35°C and 70 to 150 bar; (c) removal of an oily fraction containing the insecticidally active components as well as most of the essential oils in a second expansion step at 15 to 30°C and 40 to 70 bar; (d) removal of essential oils by steam distillation, and if desired; (e) hydrogenation of the insecticidally active components.

[22]

http://students.chem.tue.nl/6n220-8/conclusion_and_discussion.htm

[23]

patent [EP0023680](#), 1981-02-11

"**process for the production of spice extracts**"

NORBERT BEHR, HENK VAN DER MEI, WOLFGANG SIRTIL, DR HARALD SCHNEGELBERGER, DR OTHMAR VON ETTINGSHAUSEN; HENKEL KGAA

abstract: 1. a process for the production of spice extracts by extraction with a physiologically acceptable gas as a solvent in two stages, characterised in that the ethereal oils acting as odour component are removed from the spices in the first stage using a liquid gas of which the temperature is in the subcritical range and the pressure in the supercritical range whilst the flavour components are removed in the second stage using the same gas of which the temperature and pressure are both in the supercritical range, the extracts are separated off from the solutions obtained by changing the pressure and/or temperature and optionally mixed with one another.

[25]

<http://www.indianspices.com/html/s1310new.htm>

http://www-ang.kfunigraz.ac.at/~katzner/engl/generic_frame.html?Pipe_lon.html
phytochemistry 1985 24: 279

isolation of piperine

place 15g (1) of ... ground black pepper in a 250mL round-bottomed flask, add 150mL of 95% ethanol and 5 boiling chips (2), and heat at reflux for 2h. filter the mixture by suction filtration and then concentrate the filtrate to a volume of 10-15mL by simple distillation or by use of a rotary evaporator. to 10mL of a 10% solution of KOH in 95% ethanol contained in a 125mL erlenmeyer flask add the concentrated pepper extract. heat the resulting solution and add water dropwise. a yellow precipitate forms. add water until no more solid appears to form and then allow the mixture to stand at least overnight (3). collect the solid by suction filtration and recrystallize it with 10-20mL of acetone (4).

(1) this extraction may be scaled up to twice the amounts specified without difficulty. if a soxhlet extractor is available, this would be an apparatus superior to a standard reflux setup.

(2) boiling chips are necessary to prevent serious bumping.

(3) it is best to allow piperine to completely precipitate out by allowing the mixture to stand until the next laboratory period.

(4) in our hands ca. 0.6g of piperine, mp 127-128°C, was collected upon recrystallization.

[05, page 527-528]

isolation of piperine from black pepper

procedure

10g black pepper is ground to a fine powder and extracted with 150mL 95% ethanol in a soxhlet extractor for 2h. the solution is filtered and concentrated in vacuo on a water bath at 60°C. 10mL 10% alcoholic KOH solution is added ... and after a while decanted from the insoluble residue. the alcoholic solution is left overnight, whereupon 0.3g yellow needles are deposited, mp 125-126°C.

TLC of black pepper extract

the crude extract is spotted on a thin-layer plate (silica gel GF254) and developed with benzene:EtOAc 2:1.

detection:

(1) UV365 shows blue fluorescence of piperine

(2) spraying with anisaldehyde-sulfuric acid reagent, prepared by mixing 0.5mL anisaldehyde with 10mL glacial acetic acid, 85mL MeOH, and 5mL concentrated sulfuric acid. this solution is sprayed on the plate, which is then heated at 110°C for 10min. piperine appears as a yellow spot, $R_f=0.25$.

[06, page 233-236]

isolation of piperine from black pepper

piperine, a very weakly basic substance, can be isolated from a variety of peppers by extraction with alcohol. ... piperine, along with a small amount of its Z,E isomer, accounts for about 10% of the weight of black pepper.

procedure

place 15g of ground black pepper and 1g of powdered CaCO_3 (1) in a 250mL boiling flask, add 100mL of IPA, and, after fitting the flask with a reflux condenser, boil the mixture for about 1h on the steam bath. at the end of the heating period, filter the mixture by gravity into a 125mL erlenmeyer flask, clean the 250mL boiling flask, and return the filtrate to the boiling flask. fit the boiling flask with a distillation adapter and condenser, and boil off all but about 10mL of the IPA (2). transfer the residual solution from the boiling flask to a 25mL erlenmeyer flask, and set the flask aside to cool for crystallization of piperine (3,4). collect the product by suction filtration, using small portions of MeOH to rinse the flask and wash the product. yield: about 0.5g.

(1) the addition of CaCO_3 should prevent the extraction of acidic components of pepper

(2) IPA boils at 80°C , only a little below the maximum temperature attainable on the steam bath. to make the distillation proceed quickly, clamp the boiling flask so that it is well down in the rings of the steam bath, and drape a towel over the flask and the steam bath to make a tent that will hold steam around the top of the flask.

(3) crystallization occurs slowly, and the flask must be allowed to stand for at least 24h.

(4) alternatively, add 25mL of water to the IPA solution of piperine, allow the mixture to stand for at least 24h so that precipitation will be complete, collect the solid by suction filtration, and recrystallize it from either IPA or acetone.

[04, page 340-341]

isolation of piperine from black pepper

add 5g of pure ground pepper and 10mL of CH_2Cl_2 to 50mL round-bottomed flask. use the round-bottomed flask as the basis for a reflux apparatus having a water-cooled condenser and heating mantle. heat the sample to reflux, and then maintain a gentle reflux for 20min. after the required reflux period, lower the heating mantle and allow the reflux apparatus to cool for 5min. suction filter the slurry with the aid of a 4.5cm buchner funnel, washing the pepper grounds once with 5mL of CH_2Cl_2 . remove 2 or 3 drops of the extract and place it in a capped vial for use in the TLC analysis.

trituration/isolation

transfer the extract obtained above to a clean 25mL round-bottomed flask and concentrate in vacuo. the resulting olive-brown, viscous oil should be cooled in an ice-bath and then 3mL of cold ether added to the oil while gently stirring for 3-4min.

some piperine may precipitate at this point, but remove the solvent in vacuo anyway. once again cool the resulting oil in an ice-bath and then add 3mL of cold ether to the oil while gently stirring to promote the precipitation of piperine. allow the flask to cool for an additional 10min with occasional stirring. isolate the straw-yellow crystals of crude piperine by suction filtration with the aid of a 1.5cm hirsch funnel. wash the crystals twice with 2mL portions of cold ether. place a small portion of the filtrate in a capped vial for use in the TLC analysis.

recrystallization

place the crude piperine isolated above into a 13x100mm test tube and dissolve it in a minimum amount of hot 3:2 acetone:hexane solution. once all the solid has dissolved, allow the test tube to sit undisturbed for 15min at room temperature. rod-like, yellow crystals of piperine should be present. cool the solution for an additional 30min in an ice-bath before isolating the purified piperine by suction filtration with the help of a 1.5cm hirsch funnel. wash the crystals once with a 2mL portion of cold ether, allow them to air dry for several minutes. typically, yields of approximately 2% or 100mg are obtained. the melting point of the purified piperine now can be determined and the identity of the product confirmed by mixed melting point, TLC analysis, or spectral analysis.

TLC analysis

transfer a small portion of the purified crystals to a small vial and dissolve them in a drop or two of acetone. prepare a silica-gel TLC plate for the spotting of 4 samples (kieselgel 60 F254 plates having a 0.2mm coating thickness are recommended). with the aid of a capillary, place a sample of the crude oil remaining from the extraction procedure, a sample of the filtrate from the trituration/isolation procedure, the sample prepared from the purified piperine, and a sample of a piperine standard on separate points of the thin-layer plate. develop the plate using 3:2 acetone:hexane. visualize under UV illumination and stain in an iodine chamber.

[01]

isolation of natural piperine

grind 25g fresh peppercorns to a fine powder, place in a soxhlet thimble, and extract with 100mL ethanol for 90 minutes. cool the resulting solution, filter if necessary, and concentrate on the rotary evaporator. keep the water bath below 60°C during the concentration. dissolve the residue in 25mL 10% alcoholic KOH. decant the solution if any residue remains. cool the solution in an ice bath, and add water dropwise (about 30mL will be required) to precipitate the piperine. collect the piperine on a sintered glass funnel, and dry it on the vacuum pump.
... recrystallization from acetone:hexane 3:2 will produce cleaner material.

[14]

extraction and isolation

10kg dried fruits of *p nigrum l* ... were crushed and extracted 5x with EtOH at room

temp. after removal of solvent in vacuo, the syrupy residue was left overnight at room temp. when a white crystallate sept out, which was filtered. on recrystallization from MeOH it formed 50.54g fine needles, mp 128-129°, and was identified as piperine.

[19]

piperine and piperiline extraction

750g dry fruits of black pepper were ground and extracted with 2.5L ethanol, in a soxhlet apparatus for 72h. the extract was concentrated under reduced pressure in a rotary evaporator to leave 8g of a dark brown oil. this material was fractionated on a silica gel column, eluting with hexane + diethyl ether (1 + 2 by volume). the fractions obtained were combined according to their similarities as analysed by thin layer chromatography (TLC) and this led to the isolation of 2g piperine and 0.3g piperiline. these compounds were recrystallised with a mixture of dichloromethane and hexane and the physical and spectroscopic data obtained were in accordance with those reported in the literature.

[09]

piperine form piper longum

p longum ... 500g dried fruits were powdered and extracted 120h with CH₂Cl₂:MeOH 1:1. the concentrated extract (1.45g) was chromatographed over silica gel, the column being eluted with pet. ether and pet. ether-EtOAc mixture. the following compounds were eluted according to the increasing order of polarity: 120mg tridecyldihydro-*p*-coumarate, 126mg eicosanyl-(E)-*p*-coumarate, 132mg pellitorine, 67mg piperlongumine and 148mg piperine.

[35]

oleoresin of pepper

... black pepper ... ground ... berries must be extracted repeatedly(percolated) with volatile solvents: alcohol, acetone or ether. concentration of the solutions and removal of the solvent in vacuo yields the so-called oleoresin of pepper.

quantitative composition of the oleoresin depends upon the solvent used. oleoresin of pepper generally contains these compounds: 1. *piperine*, ... 2. *chavicine*, ... an isomer of piperine ... 3. *other piperidides*, ... 4. *the volatile oil*, ... 5. *a volatile alkaloid*, ... present in small quantities only. 6. *resins*, not identified.

[08, page 144]

process to recover piperine from resin of black pepper

a reaction vessel was charged with 0.9kg urea, 3.7kg ethanol (or 2.7kg methanol) and 0.3kg of the resin of black pepper to form a mixture. the mixture was refluxed for approximately 1h. the refluxed mixture was cooled overnight to 0-5°C. the cooled mixture was then filtered to remove solids (e.g wax, urea, fatty acids). the filtrate was then concentrated to obtain 180g of piperine and some unreacted urea. the 180g of piperine was recrystallized by adding ethanol. the piperine crystals were collected by filtration and dried to yield approximately 75g of 98% pure piperine.

[12]

source of piperine

black pepper oleoresin or long pepper oleoresin is used as the source of piperine. ground up black pepper or long pepper can also be used

to 35L buthanol/hexane mixture, 35kg black pepper oleoresin is added and heated to 40°C. the mixture is then cooled and filtered. the percipitate is washed with buthanol/hexane mixture to obtain crude piperine. the crude piperine is dissolved in ethanol at 60°C and treated with alumina and charcoal by stirring. it is then filtered and concentrated under vacuum to obtain a pale yellow crystalline powder, melting range: 128-131°C, min.98% pure piperine (by HPLC).

[13]

further recipes and references

with EtOH [26, (1)]

with MeOH [27]

with EtOAc: [recipe 1](#), [recipe 2](#)

with CHCl₂: [recipe 1](#) [10], [recipe 2](#)

with acetone: [[hive](#) post [282850](#) on 2002-03-15 by Antoncho]

microwave-assisted extraction of piperine from piper nigrum [15]

extraction of piperine from piper nigrum (black pepper)
by hydrotropic solubilization [31]

process for extraction of piperine from piper species [07]

extraction and description of the piperines in pepper [16]

isolation of piperine from black pepper

[<http://www.wiu.edu/users/mftkv/Chem332/Experiment3.html>]

... extracted ground black pepper with acetone ...

agricult food chem, 1981 29, 115; su, horvat

(mentioned in [21])

... piper nigrum fruit extract and its main alkaloid, piperine [17]

... pepper raw spice, oleoresins, and soluble seasonings.

piperine is extracted into ethylene dichloride ... [11]

... pepper or piper longum ... is extracted ... [34]

process for preparing piperine [02]

immersing extraction of pepper [32]

CO2 extraction, up to 9.2% piperine from black pepper(madagascar) [23]

liquid CO2 extraction of piperine ... of pepper [33]

references

[hive]

<http://www.the-hive.ws/>

[pubmed]

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>

[01]

journal of chemical education 1993 70(7): 598-599

"isolation of piperine from black pepper"

william w epstein, david f netz, jimy l seidel

[02]

patent [CN1294127](#), 2001-05-09 (chinese)

"process for preparing piperine"

xiaoming lin, zaifeng shi, zhenfan sun

(Lutianyuan Hi-Tech Development Co., Ltd., Hainan, Peop. Rep. China)

Faming Zhuanli Shenqing Gongkai Shuomingshu

abstract (from esp@cenet): a process for preparing piperine includes immersing extraction of pepper is mixed organic solvent, distilling to separate out organic solvent to obtain liquid mixture of pepper oil resin and piperine, cooling to separate out the pepper oil resin, and further purifying. Its advantages are simple process, high extraction rate and separation effect, and high purity.

abstract (from CAS): the process comprises extg. pepper with mixed solvent at 25-40° for 1-6 h, filtering, concg., crystg., and recrystg. with dichloroethylene or Et acetate. the mixed solvent is ethanol, methanol, acetone, Et ether, Et acetate, dichloromethane, benzene, and/or chloroform.

keywords (from CAS): piperine isolation pepper

[03]

[king's american dispensatory](#) 1898

m d harvey wickes felter, phr m ph d john uri lloyd

[04]

"techniques and experiments for organic chemistry" 6.edition 1998

addison ault (cornell college); universityscience books, susalito, california

ISBN 0-935702-76-8

[05]

"laboratory experiments in organic chemistry" 3.edition 1979

jerry r. mohrig, douglas c. neckers

d. van nostrand company, new york

ISBN 0-442-25471-7

[06]

"natural products - a laboratory guide" 2.edition 1991

raphael ikan; academic press, inc; ISBN 0-12-370551-7

[07]

[patent US6365601](#), 2002-04-02

"process for extraction of piperine from piper species"

RAMAN GIRIJA (IN); GAIKAR VILAS GAJANAN (IN)

COUNCIL SCIENT IND RES (IN)

abstract: the present invention relates to a process for extraction of piperine of formula I from the fruits of piper species, comprising the steps of:contacting the fruit of piper species with aqueous hydrotrope solution at a temperature in the range of 0-100 C. and separating the solution from the solid residue by known methods, and recovering piperine from the solution by known methods.

[08]

"the essential oils" volume five 1952, ernest guenther

d van nostrand company, toronto - new york - london

[09]

[pest management science 2000 56\(2\): 168-174](#)

"synthesis and insecticidal activity of new amide derivatives of piperine"

vanderlúcia fde paula, luiz c de a barbosa, antônio j demuner,

dorila piló-veloso, marcelo c picanço

abstract: the natural lipophilic amides piperine and piperiline were isolated from piper nigrum l (piperaceae). piperine was hydrolysed into piperic acid (85% yield) which was converted into 16 amides (28-89% yield). the contact toxicity of all synthetic amides, and also that of piperine and piperiline, at the dose 10 µg per insect, was evaluated for the brazilian economically important insects *ascia monuste orseis* latr, *acanthoscelides obtectus* say, *brevicoryne brassicae* l, *protopolybia exigua* de saus and *cornitermes cumulans* kollár. the results demonstrated that the insects have different sensitivities to the various amides, with mortality ranging from 0 to 97.5% according to the compound and insect species.

[10]

[phbcan99.rtf](http://www.uni-bayreuth.de/departments/oc1/teaching/phbcan99.rtf) from <http://www.uni-bayreuth.de/departments/oc1/teaching/>

"isolierung von piperin aus schwarzem pfeffer und abbau zur piperinsaeure"

ANALYTISCHES PRAKTIKUM fuer Biochemiker (Stand: September 1999), page 16-18

[11]

j assoc off anal chem 1987 70(1): 112-3

"UV spectrophotometric determination of piperine in pepper preparations: collaborative study."

t lupina, h cripps

abstract: eight collaborating laboratories performed replicate analyses for piperine on 5 samples representing pepper raw spice, oleoresins, and soluble seasonings.

piperine is extracted into ethylene dichloride and measured at maximal absorbance 342-345 nm with a UV light source. piperine content is calculated using an absorbance factor derived from piperine. Intralaboratory coefficients of variation (CVo) ranged from 0.5 to 3.1%; interlaboratory coefficients of variation (CVx) ranged from 3.0 to 5.8%. the method has been adopted as an official method of the american spice trade association and as an official first action method by AOAC.

[[pubmed](#), PMID: [3558260](#)]

[12]

patent [US6054585](#), 2000-04-25

"process for making high purity piperine for nutritional use"

muhammed majeed, vladimir badmaev; sabinsa corp

abstract: the present invention relates to a process of making high purity piperine for nutritional and nutraceutical application. this process recovers piperine from piperine-containing oleoresin by using isourea, urea or a urea derivative to remove organic matter other than piperine from the oleoresin. preferably, the process recovers piperine from oleoresin of fruit of piper nigrum or piper longum. more preferably, the process recovers piperine from oleoresin of fruit of piper nigrum, i.e. black pepper.

[13]

patents [US5744161](#), [US6054585](#), [US5972382](#), [US5536506](#)

[14]

<http://www.chemistry.uvic.ca/chem465-66/465e03piperine.pdf> from

<http://www.chemistry.uvic.ca/chem465-66/465organic.htm>

[15]

[ind eng chem res 2002 41\(10\): 2521-2528](#)

"microwave-assisted extraction of piperine from piper nigrum"

girija raman, vilas g gaikar

abstract: a novel microwave-assisted technique (MAE) for the extraction of piperine from coarsely powdered black pepper (Piper nigrum) was studied.

the parameters such as nature of the solvent, microwave energy input, and solid loading were optimized. the mechanism of the enhancement of extraction rates was investigated by microscopic studies of the irradiated material.

studies have revealed that dielectric heating of the polar cellular matrix resulted in remarkable swelling and coalescence of the oil cells and other constituents.

the resulting pressure, built-up within the cell, breaks open the cell, releasing the constituents and providing easy access for solvent penetration and subsequent solubilization of piperine and other substances. because the cell wall is mainly composed of slightly ionic cellulose, there is a marked increase in the dielectric heating rates. rapid degradation of the cellulosic cell wall occurs, thereby further increasing the permeability of the wall toward solvent penetration. selective extraction of piperine in nonpolar solvents to the extent of 94% with a purity of 85% has been achieved. the MAE procedure is simple, rapid, and reliable.

[16]

bull soc chim 1877 27(2): 290

"the extraction and description of the piperines in pepper"

p caseneuve, o caillol

[17]

planta medica 1999 65: 600-3

"stimulation of mouse melanocyte proliferation by piper nigrum fruit extract and its main alkaloid, piperine"

zhixiu lin, j r s hoult, dorothy c bennett, amala raman

abstract: during a herbal screening programme to find potential repigmenting agents for the treatment of vitiligo, piper nigrum l. fruit (black pepper) extract was found to possess growth-stimulatory activity towards cultured melanocytes. its aqueous extract at 0.1mg/ml was observed to cause nearly 300 % stimulation of the growth of a cultured mouse melanocyte line, melan-a, in 8 days ($p < 0.01$). piperine (1-piperoylpiperidine), the main alkaloid from piper nigrum fruit, also significantly stimulated melan-a cell growth. both piper nigrum extract and piperine induced morphological alterations in melan-a cells, with more and longer dendrites observed. the augmentation of growth by piperine was effectively inhibited by RO-31-8220, a selective protein kinase C (PKC) inhibitor, suggesting that PKC signalling is involved in its activity. this is the first full report on such an activity of black pepper and piperine.

[19]

[phytochemistry 1997 45\(8\): 1617-1619](#)

"an amide from fruits of piper nigrum"

bina s siddiqui, sabira begum, tahsin gulzar, farhat noor, fatima noor

abstract: a new amide, N-isobutyl amide of octadeca-trans-2-cis-4-dienoic acid has been isolated from the dried and crushed fruits of *piper nigrum*, along with the known alkaloid, piperine. complete assignments of the protons and carbons of the new amide and piperine have been made based on 2D NMR studies.

[21]

patent [US4820517](#), 1989-04-11

"process for obtaining a pepper extract with insecticidal activity"

HANS PFEIFFER, MANFRED BIERMANN, PETER SCHROEDER, GERD GOEBEL, ANNEMARIE MUELLER; HENKEL KGAA

abstract: PCT No. PCT/EP85/00333 Sec. 371 Date Jul. 24, 1986 Sec. 102(e) Date Jul. 24, 1986 PCT Filed Jul. 6, 1985 PCT Pub. No. WO86/01981 PCT Pub. Date Apr. 10, 1986. An insecticidally active fraction is obtained from black pepper by a process comprising the following steps: (a) extraction of black pepper in ground form with CO₂ at 30 to 70°C and 150 to 500 bar; (b) removal of sharp tasting fractions therein in a first expansion step at 25 to 35°C and 70 to 150 bar; (c) removal of an oily fraction containing the insecticidally active components as well as most of the essential oils in a second

expansion step at 15 to 30°C and 40 to 70 bar; (d) removal of essential oils by steam distillation, and if desired; (e) hydrogenation of the insecticidally active components.

[23]

patent [EP0023680](#), 1981-02-11

"process for the production of spice extracts"

NORBERT BEHR, HENK VAN DER MEI, WOLFGANG SIRTL, DR HARALD SCHNEGELBERGER, DR OTHMAR VON ETTINGSHAUSEN; HENKEL KGAA

abstract: 1. a process for the production of spice extracts by extraction with a physiologically acceptable gas as a solvent in two stages, characterised in that the ethereal oils acting as odour component are removed from the spices in the first stage using a liquid gas of which the temperature is in the subcritical range and the pressure in the supercritical range whilst the flavour components are removed in the second stage using the same gas of which the temperature and pressure are both in the supercritical range, the extracts are separated off from the solutions obtained by changing the pressure and/or temperature and optionally mixed with one another.

[26]

[\(1\) piperine from black pepper \(2\) hydrolysis of piperine to piperic acid](#)

<http://www.rhodium.ws/chemistry/piperine.txt>

[27]

["piperine to piperonal procedure"](#), the cook

<http://www.rhodium.ws/chemistry/piperine.txt>

[31]

[ind eng chem res 2002 41\(12\): 2966-2976](#)

"extraction of piperine from piper nigrum (black pepper) by hydrotropic solubilization"

giriya raman, vilas g gaikar

abstract: hydrotropes, such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulfate, were used for the selective extraction of piperine by cell permeabilization of piper nigrum fruits. penetration of the hydrotrope molecules into the cellular structures and subsequent cell permeabilization were hypothesized to explain the enhanced extraction rates of aqueous hydrotrope solutions. hydrotrope molecules, after adsorption on a cell wall, cause disorder in its structure and in the bilayered cell membrane to facilitate the rapid extraction of piperine. the hydrotrope solution showed selective and rapid extraction of piperine from black pepper. the recovered piperine was ~90% pure and substantially free from oleoresins. the type and nature of the hydrotrope, the hydrotrope concentration, the temperature, and the particle size all had significant effects on the extraction process.

[32]

patent [CN1294127](#), 2001-05-09

"process for preparing piperine"

SHI ZAIFENG, SUN ZHENFAN, LIN XIAOMING; LUTIANYUAN HI TECH DEV CO LTD

abstract: A process for preparing piperine includes immersing extraction of pepper in mixed organic solvent, distilling to separate out organic solvent to obtain liquid mixture of pepper oil resin and piperine, cooling to separate out the pepper oil resin, and further purifying. Its advantages are simple process, high extraction rate and separation effect, and high purity.

[33]

patent [US4985265](#), 1991-01-15

"process for extraction of spices"

DUBOC SORAYA, RENON HENRI, LAUGIER SERGE, MIZANDJIAN JEAN-LUC,
PEAN JEAN-LOUIS; L AIR LIQUIDE SOCIETY ANONYME

abstract: a process for extracting spices in liquid carbon dioxide in the presence of an alimentarily acceptable cosolvent which does not degrade the flavors of the spices. the process is particularly applicable to the extraction of piperine and aromatic compounds of pepper.

[34]

patent [CN1298936](#), 2001-06-13

"process for preparing health-care peperic acid wine"; li yueting

abstract: the present invention relates to a preparation technology of piperic-acid health-care wine which uses pepper or piper longum as raw material, and it is extracted and mixed with wine to obtain the product which not only possesses wine flavour, but also possesses the medicinal health-care active of pepper or piper longum. it can prevent the rise of blood serum cholesterol and formation of choleithiasis.

[35]

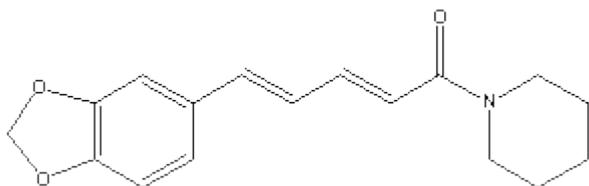
boll chim farmaceutico 1998 137(8): 319-320

"long chain esters and alkamides from piper longum"

b das, a kashinatham, p madhusudhan

abstract: from the fruits of piper longum two long chain esters, tridecyldihydro-p-coumarate and eicosanyl-(E)-p-coumarate and three alkamides, piperine, piperlongumine and pellitorine have been isolated. the first ester is a new compound and the second ester is reported for the first time from this plant.

piperine



CAS: [94-62-2]

M(C₁₇H₁₉NO₃) = 285.34 g/mol

mp 130°C

[piperine](#) [[merck index](#)]

[piperin](#) [[roempp](#)]

[piperine](#) [[beilstein/crossfire](#)]

[piperinum](#) [[kad](#)]

determination of piperine ... by TLC and UV absorption ... [[30](#)]

piperine forms a solid complex with 1,3,5-trinitrobenzene in a ratio 1:1, in the form of red needles, mp 130°C. [06, page 235]

IR analysis of piperine in black pepper [20]

further references: [piperine](#)

references

[merck index]

THE MERCK INDEX on CD-ROM / Version 12:3 / 1999

[roempp]

roempp lexikon chemie version 2.0, cd-rom,
stuttgart / new york: georg thieme verlag 1999

[beilstein/crossfire]

<http://www.mimas.ac.uk/crossfire/>

[pubmed]

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>

[kad]

[king's american dispensatory](#) 1898

m d harvey wickes felter, phr m ph d john uri lloyd

[06]

"natural products - a laboratory guide" 2.edition 1991

raphael ikan; academic press, inc; ISBN 0-12-370551-7

[20]

[IR Analysis of Piperine in Black Pepper](#)

<http://www.terrificscience.org/lessonexchange/PACTPDF/PiperineAnalysis.pdf>

[30]

chromatogr 1985 338(1): 259-63

"determination of piperine in biological tissues by thin-layer chromatography and ultraviolet absorption densitometry."

bg bhat, n chandrasekhara

[pubmed, PMID: [4019654](#)]

degradation of piperine

1g piperine and 10mL 10% alcoholic potassium hydroxide are refluxed for 90min. the ethanolic solution is evaporated to dryness under reduced pressure, the receiver being cooled in an ice-salt bath. the solid potassium piperinate is suspended in hot water and acidified with hydrochloric acid. the voluminous yellow precipitate is collected on a buchner funnel, washed with cold water, and recrystallized from ethanol to yield

piperic acid as yellow needles of mp 216-217°C. the strongly basic ethanolic distillate in the receiver is saturated with hydrochloric acid and evaporated to dryness to give piperidine hydrochloride, which melts at 244°C after recrystallization from ethanol.

[06, page 236-238]

preparation and properties of piperic acid

the cleavage of piperine was accomplished with alcoholic KOH ... numerous experiments showed us that the following procedure is the most practical and gives almost the theoretical yield. in a roomy flask connected with an ascending cooler a mixture of 1 part fine grinded piperine with 1 part KOH and 5 parts usual alcohol is boiled mildly about 24h in a water-bath.

...
in our experiments the decomposition was finished largely after 24h heating. after cooling the precipitation consisting of yellowish glossing leaflets was separated through a cheesecloth from the dark piperidine containing mother liquor, washed out with cold alcohol and recrystallized a few times from hot water under addition of animal coal. so the piperic acid potassium salt is obtained very easily pure in completely colorless, warty grouped prisms, that become again yellow colored at light. - the filtered alcoholic mother liquor gives, if boiled 24h anew with one third of the prior applied KOH amount, another small amount of very impure, dark colored piperic acid potassium salt.

...
to obtain the free acid, the potassium salt was dissolved in about 50 parts boiling water, a small excess of hydrochloric acid was brought into the solution and the whole was heated for some time. the piperic acid was obtained as a lightish sulphur-yellow, amorphous, looser precipitation. ... after the washing and drying the acid was recrystallized from boiling alcohol. for the dissolution of 1 part piperic acid about 50 parts alcohol were required.

[18, page 27-29]

hydrolysis of piperine to piperic acid and piperidine

... place 1g of piperine and 10mL of a 10% solution of KOH in 95% ethanol in a 50mL round-bottomed flask. attach a condenser and heat at reflux for 90min. attach the flask to an apparatus suitable for distillation under reduced pressure. using an aspirator distill until dryness (1) and collect the distillate in an ice cooled receiver flask. scrape the residue into a 125mL erlenmeyer flask (use water to rinse material clinging to the sides of the round-bottomed flask). suspend the residue in a total volume of about 50mL of water, heat over a steam bath, and then acidify (in the hood) with hydrochloric acid. occasionally swirl the erlenmeyer flask. collect the voluminous yellow precipitate of piperic acid by suction filtration, wash with cold water, and recrystallize from hot ethanol (2).
note the odor of the distillate. check the distillate with litmus or pH paper (3).

(1) bumping may occur at this step.

(2) the yield of crude piperic acid is high. the melting point of the recrystallized acid is 214-215°.

(3) the hydrochloride salt of piperidine may be isolated ...; however we have found this to be difficult and probably not worth the effort.

[01, page 528]

preparation of 5-(3,4-methylenedioxy phenyl)-2E,4E-pentadienoic acid (piperic acid)

piperine (28.0g, 98mmol, mp 132°C) dissolved in 200mL ethylene glycol and refluxed at 180°C after adding 25g potassium hydroxide and after the completion of the reaction the contents diluted with sufficient amount of water and acidified with 2N HCl. the resulting precipitate filtered and dried to give crude product which on crystallisation from ethanol gave piperic acid (13.8g, 65%, mp 217°C) as pale yellow solid (lit. mp 217°C).(27)

(27) dictionary of natural products 1994 4 3920; chapman, hall

[03]

preparation of piperinic acid

to piperine (2g, 0.7mmol, 1eq), 20% of methanolic KOH (100mL) was added and refluxed for 2days. after completion of the hydrolysis, methanol was removed under reduced pressure and a yellow coloured oily solid was obtained. this residue was dissolved in 50mL water and acidified with 6N HCl to pH<1 yielding a yellowish precipitate of piperinic acid. recrystallization from methanol gave yellow needles (0.9g, 60% yield). mp 206°-208°C (lit mp 217°-218° (1))

(1)

tetrahedron 1967 23: 1769-1781

"alkaloids of piper longum linn-I structure and synthesis of piperlongumine and piperlonguminine"

a.chatterjee, c.p.dutta

[02, page 69(60), 76(67)]

preparation of piperic acid

in a 1L round-bottom flask was placed 6g piperine, 500mL ethanol and 100mL aqueous LiOH 90g/L solution. the resultant solution was refluxed for 140h, and the reaction was then quenched by addition of 35mL concentrated hydrochloric acid. the solid formed was removed by filtration and recrystallized from THF to produce piperic acid in 85% yield, mp 126-127°C.

[09]

(mp 126-127°C looks like an error. it seems that 1 and 2 are permuted. other papers report mp 216-217°C. also 140h sounds extremely long [3base])

further recipes and references

[piperic acid - beilstein/crossfire search as product](#)

[degradation of piperine to piperic acid with KOH in MeOH/H2O](#) (german)

hydrolysis of piperine to piperic acid [26, (2)]

hydrolyze with NaOH in alcohol. (MeOH/EtOH both verified) [27]

hydrolysis of piperine to piperic acid and piperidine [28]

piperine ... alkaline hydrolysis ... 2N KOH in diethylene glycol and reflux 2h [29]

the present invention relates to a preparation technology of piperic acid ... which uses pepper or piper longum ... [34]

references

[01]

"laboratory experiments in organic chemistry" 3.edition 1979

jerry r. mohrig, douglas c. neckers
d. van nostrand company, new york
ISBN 0-442-25471-7

[02]

patent [GB2370989](#), 2002-07-17

"piperine analogues for the treatment of skin conditions"

VENKATASAMY RADHAKRISHNAN, RAMAN AMALA, HIDER ROBERT CHARLES
BTG INT LTD

[page 69\(60\)](#)

[03]

[bioorganic & medicinal chemistry 2000 8\(1\): 251-268](#)

"structure-activity relationship of piperine and its synthetic analogues for their inhibitory potentials of rat hepatic microsomal constitutive and inducible cytochrome P450 activities"

Surrindera Koul, Jawahir L.a Koul, Subhash C.a Taneja, Kanaya L.a Dhar, Deshvir S.b Jamwal, Kuldeepb Singh, Rashmeet K.b Reen, Jaswantb Singh

[06]

"natural products - a laboratory guide" 2.edition 1991

raphael ikan; academic press, inc; ISBN 0-12-370551-7

[09]

[pest management science 2000 56\(2\): 168-174](#)

"synthesis and insecticidal activity of new amide derivatives of piperine"

vanderlúcia fde paula, luiz c de a barbosa, antônio j demuner, dorila piló-veloso, marcelo c picanço

abstract: the natural lipophilic amides piperine and piperiline were isolated from *piper nigrum* l (piperaceae). piperine was hydrolysed into piperic acid (85% yield) which was converted into 16 amides (28-89% yield). the contact toxicity of all synthetic amides, and also that of piperine and piperiline, at the dose 10 µg per insect, was evaluated for the brazilian economically important insects *ascia monuste orseis* latr, *acanthoscelides obtectus* say, *brevicoryne brassicae* l, *protopolybia exigua* de saus and *cornitermes cumulans* kollar. the results demonstrated that the insects have different sensitivities to the various amides, with mortality ranging from 0 to 97.5% according to the compound and insect species.

[18]

analen der chemie und pharmacie 1869 152: 25-58

"untersuchungen ueber die constitution des piperins und seiner spaltproducte piperinsaure und piperidin - erste abhandlung"

rud fittig, w h mielck

[26]

[\(1\) piperine from black pepper \(2\) hydrolysis of piperine to piperic acid](#)

<http://www.rhodium.ws/chemistry/piperine.txt>

[27]

["piperine to piperonal procedure"](#), the cook

<http://www.rhodium.ws/chemistry/piperine.txt>

[28]

["piperonylic acid from black pepper"](#)

"laboratory experiments in organic chemistry", page 527

mohrig, neckers

<http://www.rhodium.ws/chemistry/piperine.txt>

[29]

[j agric food chem 1966 14\(5\): 469-472](#)

"ANALYTICAL METHOD - Determination of the Pungent Constituents of *Piper nigrum*"

BART LABRUYERE

[34]

patent [CN1298936](#), 2001-06-13

"process for preparing health-care piperic acid wine"; li yueting

abstract: the present invention relates to a preparation technology of piperic-acid health-care wine which uses pepper or piper longum as raw material, and it is extracted and mixed with wine to obtain the product which not only possesses wine flavour, but also possesses the medicinal health-care active of pepper or piper longum. it can prevent the rise of blood serum cholesterol and formation of cholelithiasis.

via KMnO_4

piperic acid \rightarrow piperonal

KMnO_4 , alkali, 3°C

byproducts: piperonylic acid, racem. 2,3-dihydroxy-succinic acid, oxalic acid

[18], [03], [24]

via Br_2 and NaOH

piperic acid $\xrightarrow{\text{Br}_2}$ tetrabromopiperic acid $\xrightarrow{\text{NaOH}}$ piperonal

... piperic acid ... reacts quickly with Br_2 in CCl_4 without forming of HBr to a compound with the molecular formula $\text{C}_{12}\text{H}_{10}\text{Br}_4\text{O}_4$... [07, page 877]

... piperic acid ... addition occurred when bromine was added ... tetrabromopiperic acid ($\text{C}_{12}\text{H}_{10}\text{Br}_4\text{O}_4$, mp $160\text{-}165^\circ\text{C}$) resulted when bromine in carbon disulfide was the reagent. ...

hot sodium hydroxide converted the tetrabromo acid to piperonal ... [04]

nitrosation of piperine

... we have nitrosated piperine using HN_2O , NOCl and N_2O_4 . the compounds identified from the nitrosation of piperine are piperonal ... [05]

references

[03]

analen der chemie und pharmacie 1874 172: 134-167

"untersuchungen ueber die constitution des piperins und seiner spaltproducte piperinsaure und piperidin - vierte abhandlung"

rud fittig, w h mielck

[04]

leo marion, II. the pepper alkaloides, 1. piperine, p.168,

the alkaloids, chemistry and physiology, volume I,
academic press inc, publishers, new york, 1950

[05]

[j agric food chem 1992 40\(11\): 2211-2215](#)

**"nitrosation of piperine using different nitrosating agents:
characterization and mutagenicity of the products"**

narmada r shenoy, ahmed s u choughuley, tulsi k shetty, rathin k bhattacharya

abstract: piperine, an N,N-disubstituted amide possessing a methylenedioxy moiety, is the main pungent principle of pepper, a spice consumed by people throughout the world. on nitrosation the reaction mixture exhibits mutagenic activity toward salmonella typhimurium strains. in the present work we have nitrosated piperine using nitrous acid (HN02), nitrosyl chloride (NOCl), and dinitrogen tetroxide (N2O4). the compounds identified from the nitrosation of piperine are piperonal (PA), 6-nitropiperonal (NPA), 3,4-(methylenedioxy)cinnamaldehyde (MDCA), 1- [5-(1,3-benzodioxol-6-nitro-5-yl)-l-oxo-2(E),4(E)-pentadienyl]piperidine (MNAP), 1- [5-(1,3-benzodioxol-5-yl)-l-oxo-2-nitro-2(E),4(E)-pentadienyl] - piperidine (MNOP), 1- [5-(1,3-benzodioxol-6-nitro-5-yl)-l-oxo-2-nitro-2(E),4(E)-pentadienyl]piperidine (DNP), and N-nitrosopiperidine (NPIP). the mutagenicity of the unfractionated nitrosated reaction mixture (UPNM) and compounds NPA, MNAP, MNOP and DNP toward S. typhimurium TA 98 and TA 100 strains was studied. compounds NPA and DNP and the unfractionated reaction mixture were found to be mutagenic toward both the strains.

[07]

"Lehrbuch der organischen chemie", 2.berichtigte auflage 1983

robert t morrison, robert n boyd; verlag chemie, weinheim; ISBN 3-527-25761-6

[18]

analen der chemie und pharmacie 1869 152: 25-58

**"untersuchungen ueber die constitution des piperins und seiner
spaltproducte piperinsaeure und piperidin - erste abhandlung"**

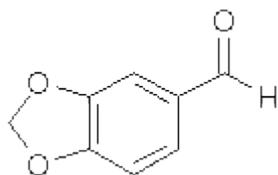
rud fittig, w h mielck

[24]

berichte der deutschen chemischen gesellschaft 1890 23: 2372-2377

"ueber die bildung von traubensaeure durch oxydation ungesaettigter saeuren"
o doebner

piperonal



CAS: [120-57-0]

[piperonal](#) [[merck index](#)]

[piperonal](#) [[roempp](#)]

purification of piperonal [[01](#)]

references

[merck index]

THE MERCK INDEX on CD-ROM / Version 12:3 / 1999

[roempp]

roempp lexikon chemie version 2.0, cd-rom,
stuttgart / new york: georg thieme verlag 1999

[01]

[patent JP8099971](#), 1996-04-16

"purification of piperonal"

HARADA KATSUMASA, SUGIYAMA TOMOSHI; UBE IND LTD

abstract:

PURPOSE: to obtain nitro compound-free piperonal as a product of high purity by oxidizing 3,4-methylenedioxymandelic acid with nitric acid.

CONSTITUTION: in the purification of piperonal formed by nitric acid oxidation of 3,4-methylenedioxybenzene which is synthesized from 1,2-methylenedioxybenzene and glyoxylic acid, the reaction mixture containing piperonal is treated with a sulfite salt and the piperonal sulfite is rinsed with an organic solvent, then the salt is decomposed with an acid or a base to regenerate piperonal.