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Kang ZHANG
Lanosterol vs Cataracts

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http://www.rt.com/usa/310909-cataract-dissolving-eyedrops-study/
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Scientists create eye drop that dissolves cataracts with naturally occurring chemical

Getting rid of cataracts normally means surgery to remove them. But researchers have discovered that a naturally occurring chemical in the human body may dissolve the blinding cloudiness when used as an eye drop.

Cataracts ? or a clouding of the eye lens ? are caused by proteins clumping together blurring their victims' vision and, if left untreated, eventually leading to blindness, according to the National Eye Institute (NEI). They affect 17 percent of Americans age 40 and older and more than half of those age 80 and older. Worldwide, tens of millions of people are affected, making cataracts the leading cause of blindness. Cataracts are initially treated with new eyeglasses, brighter lighting, anti-glare sunglasses or magnifying glasses.

"If these measures do not help, surgery is the only effective treatment," NEI notes. "Surgery involves removing the cloudy lens and replacing it with an artificial lens."

But Dr. Kang Zhang, a professor of ophthalmology at the University of California, San Diego (UCSD), thinks he may have found a different solution. His research has focused on lanosterol, a naturally occurring steroid that the human body already produces.

But Dr. Kang Zhang, a professor of ophthalmology at the University of California, San Diego (UCSD), thinks he may have found a different solution. His research has focused on lanosterol, a naturally occurring steroid that the human body already produces.

He and his team at UCSD's Shiley Eye Institute studied two Chinese families in which the children had congenital cataracts, meaning that they were the result of a genetic defect, rather than age-related. They found that the kids with the congenital version had two copies of a mutation in the gene that produces lanosterol, but their parents did not have the same mutation. Normally, the gene produces the steroid, which prevents the cataract-causing proteins from clumping together. But the mutation caused an abnormality in the lanosterol, which allowed the cataracts to form.

"By screening families across the world for mutations that affect vision, we found four kids in two families with genetic aberrations in an enzyme called lanosterol synthase," said Zhang, according to PBS 'Newshour'.

The researchers concluded that the steroid had a connection with the appearance of cataracts ? or the lack thereof. They then created an eye drop that contains lanosterol, which they first tested on

rabbits that had cataracts. To test the drops, the scientists isolated the cloudy lenses from the animals and placed them in a lanosterol solution for six days.

The rabbits' lenses became clearer and the severity of the cataracts were reduced after treatment, Zhang's team found. The lanosterol solution had an effect on 11 of the 13 animals.

"We went on to test the effect of the eye drops in dogs with cataracts. We gave them eye drops twice a day for six weeks and found it had reduced the effect of cataract severity," Zhang told IFLScience.

The researchers used seven dogs from breeds that are naturally prone to cataracts, including black Labrador retrievers, Queensland heelers, and miniature pinschers. Of the seven, three dogs' vision was cleared by the eye drops, while the other four showed improvement after six weeks of treatment.

"We saw an increase in the lens transparency and also decreased cloudiness of the cataract," Zhang said.

Because the study only lasted for a few months, the cataracts are likely to redevelop, he told IFLScience.

Zhang's next step is to figure out exactly how the eye drops work to dissolve cataracts, and then to begin human trials, Digital Journal reported.

Ophthalmologists not involved with the study said that the eye drops could become an extremely important tool in battling cataracts.

"It would have a huge public health impact," Dr. Robert B. Bhisitkul, a professor of ophthalmology at the UC San Francisco School of Medicine and who was not involved in the research, told the Los Angeles Times. "Preventing or reversing cataracts with an eye drop has been the Holy Grail in ophthalmology since the field began."

Dr. Manuel Datiles, a senior investigator and attending ophthalmologist at NEI, which is part of the National Institutes of Health ? expressed cautious optimism at how the lanosterol solution might change the field, but warned that the drops won't be able to replace surgery, at least not immediately.

"You cannot compare the improvements shown in this study with surgery. With cataract surgery, you become 20 years old again; with this one the lens is cleared up, but your vision can still be murky," he told IFLScience.

He added that lanosterol isn't the only way that researchers are trying to alleviate cataracts.

"There are other drops that do the same thing but use different pathways. This is why we need multifunctional anti-cataract agents that work together across multiple pathways to clear the lens," Datiles said. "There's now scope to investigate how we can combine this drug with other ones to better improve treatment."

Zhang's results were published in the journal Nature.

http://www.nature.com/nature/journal/vaop/ncurrent/full/nature14650.html
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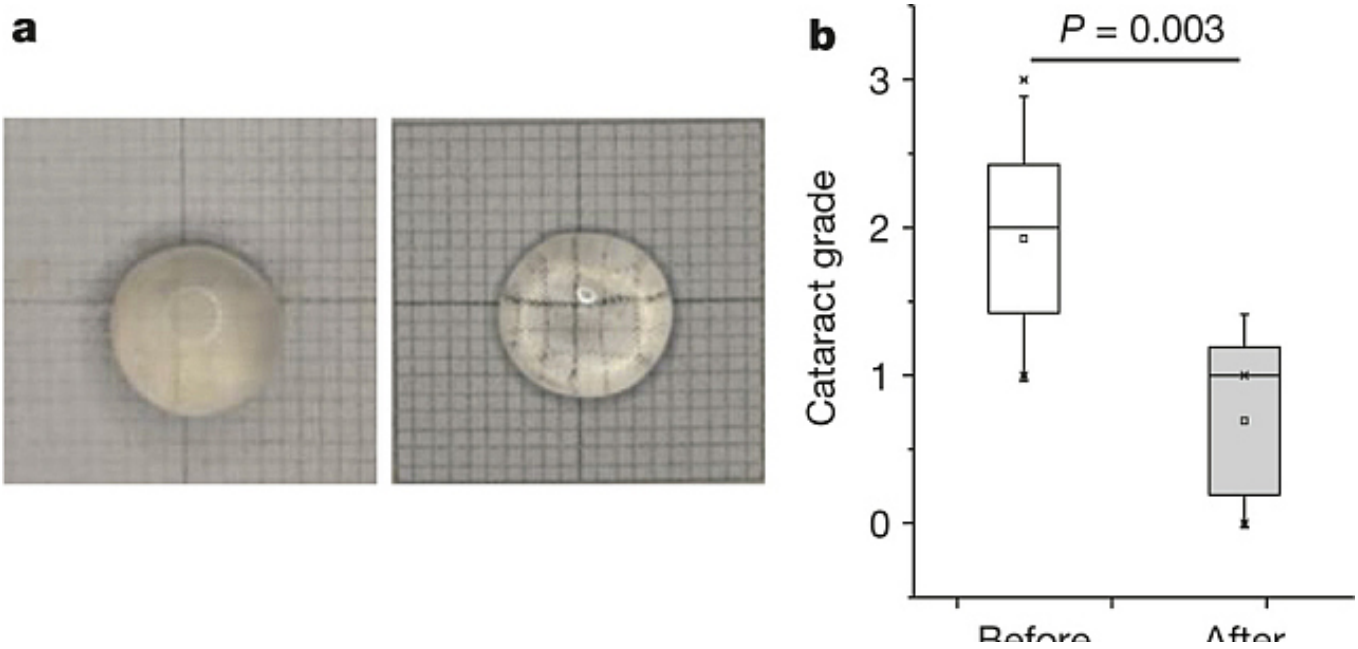
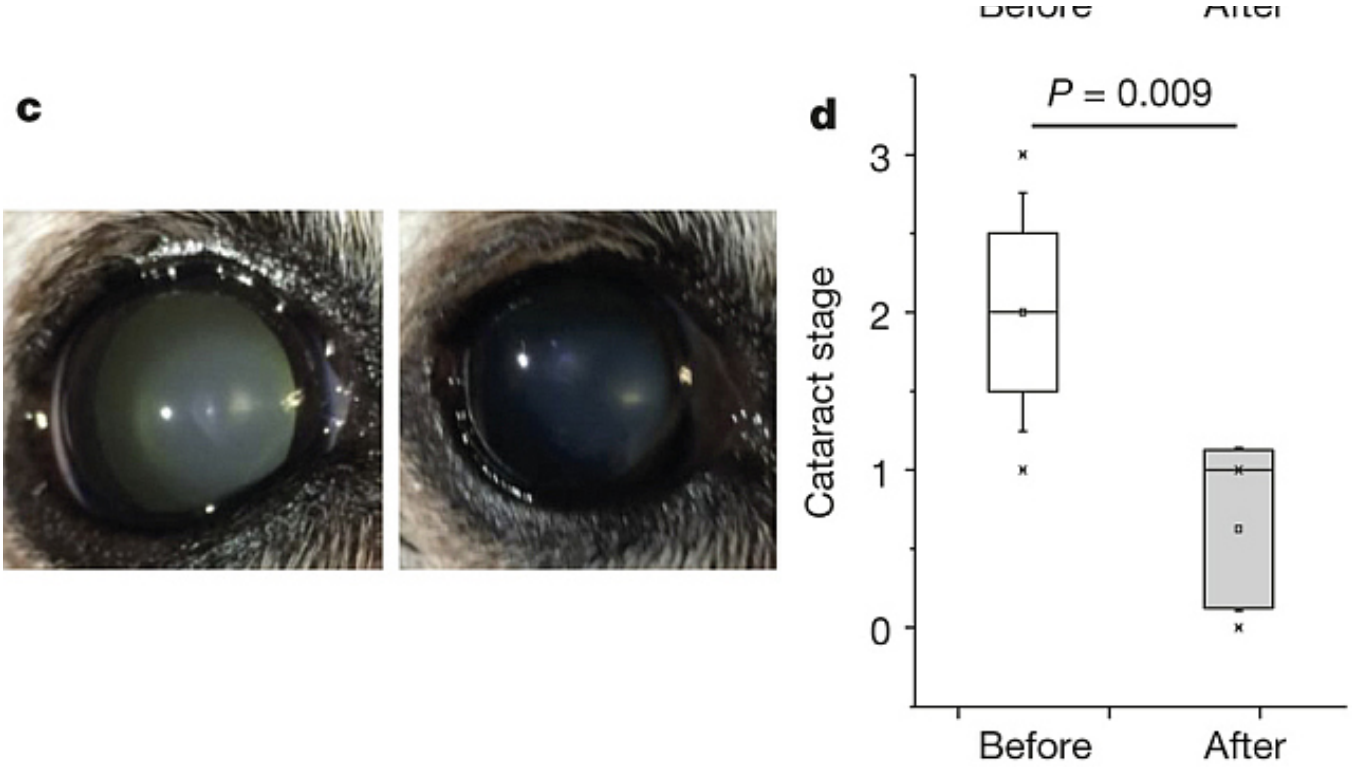
Lanosterol reverses protein aggregation in cataracts

Ling Zhao, Xiang-Jun Chen, Jie Zhu, Yi-Bo Xi, Xu Yang, Li-Dan Hu, Hong Ouyang, Sherrina H. Patel, Xin Jin, Danni Lin, Frances Wu, Ken Flagg, Huimin Cai, Gen Li, Guiqun Cao, Ying Lin, Daniel Chen, Cindy Wen, Christopher Chung, Yandong Wang, Austin Qiu, Emily Yeh, Wenqiu Wang, Xun Hu, Seanna Grob , et al.

The human lens is comprised largely of crystallin proteins assembled into a highly ordered, interactive macro-structure essential for lens transparency and refractive index. Any disruption of intra- or inter-protein interactions will alter this delicate structure, exposing hydrophobic surfaces, with consequent protein aggregation and cataract formation. Cataracts are the most common cause of blindness worldwide, affecting tens of millions of people1, and currently the only treatment is surgical removal of cataractous lenses. The precise mechanisms by which lens proteins both prevent aggregation and maintain lens transparency are largely unknown. Lanosterol is an amphipathic molecule enriched in the lens. It is synthesized by lanosterol synthase (LSS) in a key cyclization reaction of a cholesterol synthesis pathway. Here we identify two distinct homozygous LSS missense mutations (W581R and G588S) in two families with extensive congenital cataracts. Both of these mutations affect highly conserved amino acid residues and impair key catalytic functions of LSS. Engineered expression of wild-type, but not mutant, LSS prevents intracellular protein aggregation of various cataract-causing mutant crystallins. Treatment by lanosterol, but not cholesterol, significantly decreased preformed protein aggregates both in vitro and in cell-transfection experiments. We further show that lanosterol treatment could reduce cataract severity and increase transparency in dissected rabbit cataractous lenses in vitro and cataract severity in vivo in dogs. Our study identifies lanosterol as a key molecule in the prevention of lens protein aggregation and points to a novel strategy for cataract prevention and treatment.





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http://www.latimes.com/science/sciencenow/la-sci-sn-cataracts-drops-20150722-story.html

Genetics study points toward eyedrop treatment for cataracts

by

Eryn Brown

In coming decades, doctors might be able to treat or prevent cataracts with eyedrops -- all because of an unexpected discovery, revealed during a genetics study, about a molecule that helps make cholesterol in human cells.

Lanosterol, as the substance is known, can reverse the accumulation of proteins in the lens of the eye that appear to cause cataracts, UC San Diego researcher Dr. Kang Zhang and colleagues discovered.

The results of the team's work were published Wednesday in the journal Nature, and may hold promise for the tens of millions of people around the world who suffer from cataracts. Currently, the disease is treatable only through surgical removal of the lens. But potentially, thanks to the lanosterol discovery, patients might someday be able to prevent or treat the disease by using eyedrops or getting an injection -- avoiding the risks, discomfort and costs of surgery and recovery.

"It would have a huge public health impact," said Dr. Robert B. Bhisitkul, a professor of

ophthalmology at the UC San Francisco School of Medicine who was not involved in the research. "Preventing or reversing cataracts with an eyedrop has been the Holy Grail in ophthalmology since the field began."

Zhang, who is well known for his research on retinal diseases, had no idea that he'd be investigating lanosterol as part of the study.

"It was a surprise," he said.

Preventing or reversing cataracts with an eyedrop has been the Holy Grail in ophthalmology since the field began. - Dr. Robert B. Bhisitkul, UC San Francisco ophthalmologist

The work began as an investigation of the genetics in a single family in which two parents without cataracts, who happened to be first cousins, had four children: three with cataracts and one without.

Sequencing and analyzing the genomes of the parents and the children, Zhang and his team were able to zero in on a likely cause of the diseased kids' cataracts -- each had two copies of a mutated version of a gene called LSS, which was known to be involved in the production of lanosterol. (The researchers later found a second family with cataracts that also had a mutation in the LSS gene.)

To see if a problem producing lanosterol was involved in causing cataracts somehow, the researchers conducted a number of tests, introducing various types of cataract-like crystalline protein mutations into human lens cells in lab dishes and seeing whether adding lanosterol would clear them away. It did.

The team also administered the lanosterol to naturally occurring cataracts in rabbit lenses that had been incubated in lab dishes. That, too, increased the clarity of the lens. Last, the researchers treated dogs with naturally occurring cataracts with a shot of lanosterol in the eye, followed by eyedrops twice a day for six weeks. Again, lens clarity improved.

Khang said that the team next would prepare for human trials, and that he expected toxic effects of lanosterol to be "minimal," since the substance is already produced by the human body. Bhisitkul said that treatments woudn't be available until far in the future, but that he thought the greatest opportunity might lie in prevention -- that patients might start using an eyedrop when they're in late middle age, for instance, to prevent cataract formation later on.

In an editorial published alongside the study in Nature, J. Fielding Hejtmancik of the Ophthalmic Genetics and Visual Function Branch of the National Eye Institute in Rockville, Md., who was not involved in the study, noted that the world's aging population has been predicted to double the need for cataract surgeries over the next 20 years -- making the possibility of a drug-based alternative especially attractive.

"The potential for this finding to be translated into the first practical pharmacological prevention, or even treatment, of human cataracts could not come at a more opportune time," he wrote.

PATENTS

Method for separating and extracting cholesterol in lanolin alcohol CN101817859

The invention relates to a method for separating and extracting cholesterol in lanolin alcohol, which comprises the following steps: carrying out molecular distillation on lanolin alcohol, collecting the light-phase fraction which is refined lanolin alcohol, heating the refined lanolin alcohol in a mixed solvent of methanol and acetone until the refined lanolin alcohol is completely dissolved, and cooling to cooling temperature, wherein the remainder of the filtrate after reduced pressure distillation is the primary concentrate of cholesterol; heating to dissolve the primary concentrate of cholesterol in acetone, cooling to precipitate, filtering, and carrying out reduced pressure distillation on the filtrate to recover the solvent, wherein the balance is the secondary concentrate of cholesterol; heating to dissolve the secondary concentrate of cholesterol in an alcohol solvent, cooling to cooling temperature, keeping the temperature for 6-12 hours, and vacuum-filtering to obtain the white acerose cholesterol crude product; and recrystallizing the cholesterol crude product through a methanol-acetone mixed solvent to obtain the refined cholesterol product. The refined cholesterol product selectively recrystallizes through the solvent to obtain the byproduct lanosterol accounting for 63-70% and the cholesterol product of which the purity is more than 90%.

TECHNICAL FIELD
[0002]

The present invention relates to the technical field of separation and extraction of cholesterol, particularly to a method for separating and extracting lanolin alcohol, cholesterol.
[0003]

Background technique
[0004]

Cholesteric aliases cholesterol, its oxidation product 7-dehydrogenation cholesterol, in the skin by ultraviolet radiation in sunlight synthesis of vitamin D3, and therefore is an important source of vitamin D3 in the body; its unique biological properties and chiral features, as its skeleton prepared cholesteric liquid crystal is an important part of them, it has special optical properties make it in many areas and a variety of display devices and other optical components with a wide range of applications; natural biological activity of the cholesterically can be used in cosmetics play emollient, sunscreen, shrink pores, reduce wrinkles and make skin restore elasticity effect.
[0005]

Lanolin is a product of lanolin alcohol after saponification, contains 20 to 30 percent of cholesterol, 25 to 30 percent of the three terpene alcohol is an important source of natural steroids.
[0006]

Current methods of separation of cholesterol from lanolin alcohol mainly with, chromatography, supercritical fluid, solvent extraction and solvent selective crystallization.
[0007]

Patent document CZ 237195 (1983) and PL 164762 (1992) reported the application of metal chlorides (calcium chloride, magnesium chloride and zinc chloride) and formation of complexes of sterols, after hydrolysis in a solvent complexes can be precipitated out get cholesteric technology.

Although the law has industrial production value, but lanolin alcohol other alcohols containing ß-OH complexes can be formed, whereby cholesterol is not high purity obtained by hydrolysis, resulting cholesteric tedious process yield is not high. And the application of a large metal chloride, the production process will produce difficult to handle waste water containing metal ions, pollute the environment.
[0008]

After washing under Chinese patent ZL 200410025654.6 by the alcohol solution will lanolin alcohol or a halogenated hydrocarbon solution, quality lanolin alcohol has been greatly improved under the premise of direct crystallization of cholesterol.

The Act requires repeated extraction, solvent consumption is large, low yield, and the industrial extraction process scale-assessment needs to run longer.
[0009]

European Patent EP 53415 (1982) and U.S. Patent No. US 4977243 (1990) by column chromatography lanolin alcohol, cholesterol, such as silica gel as adsorbent, heptane - acetone as eluent, a column temperature of room temperature to 60 ? elution was carried out, it can be more than 67% of the crude cholesterol, after a recrystallization cholesteric a purity above 90%. Chinese Patent CN 1958596A ?- activated alumina or silica gel or macroporous resin as adsorption medium, a mixture of petroleum ether and toluene elution eluent do, you can get content to 90% of the cholesteric crude.

Chromatography to obtain high purity cholesterol, but solvent consumption, a small amount of processing, the Act is limited to small-scale production.
[0010]

Chinese Patent CN 101074257A reported in the supercritical fluid method was applied to wool alcohol separation and extraction of cholesterol in order to lower alcohols, acetone, hexane, etc., and as entrainer, extraction pressure 12 ~ 40MPa, extraction temperature 40 ~ 80 ?, extraction time 120 ~ 480min, extraction kettle residue of cholesterol concentrate recrystallized after more than 90% of the content of cholesterol.

Short process of the law, without a large number of organic solvents, but the supercritical fluid equipment investment, high operating costs.
[0011]

METHOD FOR PRODUCING STEROLS - LANOSTEROL AND CHOLESTEROL FROM WOOLY FAT
RU2283318

FIELD: medicinal industry, sterols. ^ SUBSTANCE: invention relates, in particular, to the improved method for producing sterols - lanosterol and cholesterol from wooly fat that can be used in preparing medicinal and cosmetic preparations. Method is carried out by alkaline hydrolysis of raw, extraction of unsaponifiable substances, removal of solvent and successive isolation of lanosterol and cholesterol. Alkaline hydrolysis of raw is carried out with a mixture of ethanol, sodium hydroxide, pyrogallol and water at temperature 70 DEG C for 4 h at stirring in the following ratio of components: raw : ethanol : sodium hydroxide : pyrogallol : water = 100.0: (300.0-350.0):(30.0-35.0):(0.01-0.05):(7.5-12.0), respectively, with the indicated mixture with addition of toluene in the following ratio: raw : ethanol : sodium hydroxide : pyrogallol : toluene : water = 100.0:(220.0-255.0):(30.0-38.0):(0.05-0.12):(100.0-137.0):(2.5-7.0), respectively, and lanosterol is isolated by precipitation from mixture of methylene chloride and ethanol in the ratio = 1:1. Before removal of solvent unsaponifiable substances are extracted at temperature 50 DEG C for 2-3 h at stirring. Invention provides increasing yield of the end product, enhancing qualitative indices and reducing cost of production. ^ EFFECT: improved producing method.
