

**The effectiveness of leaf extract cherry (*Muntingia calabura L.*) as lowering cholesterol levels in white rats with simvastatin comparison**

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Corresponding author e-mail:** cutmah57@gmail.com*Received on: 07-04-2017; Revised on: 09-06-2017; Accepted on: 22-06-2017ABSTRACT**

The flab in the body partly will form the excessive cholesterol, which can thicken the blood and the formation of thrombus in the blood can cause coronary heart disease, and even death are currently on the market have been widely circulated synthetic chemical drugs to lower blood cholesterol levels, but often cause various side effects, so it is necessary to find an alternative drugs from natural materials rational lowering cholesterol levels with relatively minor side effects. One plant has been used traditionally community to reduce body fat (obesity) is a cherry leaf. In addition cherry leaves have also been used to treat gout, diabetes, and high blood pressure, so that the possibility can be used as an alternative to cholesterol-lowering drugs. Extraction is done by percolation using 80% ethanol. Phytochemical screening performed on fresh leaves, botanicals, and cherry leaf ethanol extract. Decreased effectiveness of cholesterol using cholesterol level gauges Nesco@multicheck, the male rats induced by high cholesterol feed is duck eggs yolk mixture to 80% and 0.125% propylthiouracil orally by 4 ml, for 10 days to an increase in levels of blood cholesterol. Measurements were made once every 24 hours after the suspension of the ethanol extract of leaves of cherry with three doses of 2%, 4%, 6%, respectively 2 ml, as a blank CMC suspension 0.5%, and the comparison simvastatin dose of 0.025% respectively 4 ml. The data obtained were analyzed by analysis of variance (ANOVA) followed by analysis of Least Significant Difference Test (BNT) using the least squares difference (Least Square Difference) with a 99% confidence level. Phytochemical screening result looks the same class of chemical compounds on fresh leaves, botanicals, and cherry leaf ethanol extract, namely alkaloids, flavonoids, tannins, triterpenoids / steroids; and essential oils. The result of a decrease in blood cholesterol seen rats started on the third day after the administration of test materials, and showed a significant decrease in cholesterol on the seventh day, did not differ between the test material 4% and 6%. As for the test material 2%, is showing a decline on the ninth day. Of the three doses given cherry leaf extract noticeable decrease in blood cholesterol levels the most excellent rats at concentrations of 4% for the seventh day was not significantly different from the concentration of 6%.

Key words: Ethanol extract of leaves of cherry, Phytochemical screening, simvastatin, Decrease in cholesterol levels

INTRODUCTION

Cholesterol is an essential component of all cell membrane structure and is a major component of brain and nerve cells. Cholesterol is present in high concentrations in glandular tissue and in the liver where cholesterol is synthesized and stored. Cholesterol is an essential ingredient in the formation

of steroids, such as bile acid, folic acid, adrenal cortex hormones, estrogen, androgen and progesterone. Cholesterol is continuously synthesized in the liver which is about 70% of cholesterol in the blood is the result of synthesis in the liver, while 30% was donated by the intake of food. If the amount of cholesterol in the blood is still disproportionate to the needs of the body will remain healthy, but with the

development of the lifestyle of the people who tend to consume a lot of fatty food is cholesterol in the body is higher than the level of needs, which will cause various health problems, including another problem occurred coronary cardiac disease.

Various cholesterol-lowering drugs is circulated on the market, but it often contain synthetic chemicals cause a variety of adverse health effects, so it is necessary to find an alternative drug from natural ingredients to lower blood cholesterol levels by side effects are relatively mild. One of the natural substances from plants that have frequently been used traditionally to lower blood cholesterol is a cherry leaf. In addition cherry leaves have also been used to treat gout, diabetes, relieve flu symptoms, seizures or stiffness in the digestive tract due to gastritis and diarrhea, as an antibacterial or antiseptic, anti-tumor, increase endurance, relieve headaches.

Plants cherry or cherry (*Muntingia calabura L.*) is a plant species that is trunked wet and lush, easy to breed in the fertile soil and is often used as a place of shade on road verges, often grows wild in roadside ditches, or appear in the center of cracks floor walls or fences, and finally grow rapidly, usually left enlarges as a shade plant. Viewed from a variety of cherry leaf properties that have been used traditionally society, especially in the form of decoction has been proven empirically as lowering body fat and cholesterol reduction then it is very likely to be developed as a blood pressure-lowering, but no studies to prove it scientifically. The use of cherry leaf decoction is less practical and necessary volume in large quantities, as well as tough on the use, storage and distribution, it is more practical to be better prepared in extract form. Similarly, the research effectiveness as antihypertensive attempted in animal experiments administration certainly needed with the smallest possible volume, it is necessary to be made in the form of extracts to minimize a given volume.

In making the extract, it is through several stages of the process, from the drying up of making extracts that slowly will damage or loss of contents class of chemical compounds, and to make sure the presence of chemical compounds in the extract needs to be done phytochemical screening of fresh leaves, bulbs dry and ethanol extracts. Based on the researchers to test the phytochemical screening of fresh leaves, botanicals and extracts of ethanol cherry, and test the effectiveness of the ethanol extract of leaves of cherry as lowering blood cholesterol in animal experiments male rats induced to raise cholesterol by feeding high cholesterol or a mixture 80% duck egg

yolk and 0.125% propylthiouracil orally by 4 ml, for 10 days to an increase in levels of blood cholesterol.

Cherry Plant: Cherry is a plant shrubs or trees, high up to 12 m, although generally only about 3-6 m only, evergreen and continuous flowering and fruiting throughout the year. Branches horizontally, hang on the end; forming leafy shade. Smooth-haired twigs mixed with glandular hairs; as well as the leaves. The leaves lie flat, alternate; the leaf blade is not symmetric, circular egg lancet, jagged edges and sharp pointed, 1-4 × 4-14 cm, the bottom side of the gray-haired meeting; short-stemmed. Stipule the next tapered thread form, approximately about 0.5 cm, a little longer and then dry up and fall off, while ten more rudimentary. Cherry flowers appear among the foliage, in a file, containing 1-3 (-5) florets, located in the armpit rather on the growing leaf; long-stemmed; androgynous and around 5; petal share in, Taju tapered thread shape, smooth-haired; Average edged crown, inverted egg round, thin white, bald, lk 1 cm. Stamens numerous from 10 to more than 100 strands. Blooming flower is jutting out, up strands of leaves; but after the fruit hanging down, hidden under leaves. Generally, only one or two flowers become fruit in each file.

The fruit is in the form of long-stemmed, almost perfectly round, 1-1.5 cm diameter, green, yellow and finally red when ripe, crowned with the rest of the stalk pistil is not falling like black five-pointed star. Contains several thousand seeds are small, smooth, yellowish white; immersed in flesh and sweet juice once. It has colored red fruit and sweet is hidden under the leaves. Cherry fruit favored especially by children, birds and Flying-Fox. Children used to climb the tree, leaving scars in the form of broken branches and peeling bark. The fruit may also be used as a jam. In Mexico, the cherry is sold in market. Cherry in Indonesia is easy to find and usually used as a shade tree.



Fig.1: Plants cherry and cherry crop Pieces
The Benefit of Cherry Leaf

Some benefits of Cherry for health are to treat uric acid, diabetes, influenza, infection, convulsions and stiff caused by gastritis and diarrhea, and as anti-bacterial, anti-septic, high blood pressure reducer, cholesterol level reducer, anti-tumor, increasing body endurance so not easy to be sick, relieve headaches, heal cough, and overcoming inflammation.

Taxonomy of Cherry Plant

In plants systematic, cherry is classified as: (Wikipedia Bahasa Indonesia, ensiklopedia):

Kingdom : Plantae (Plants)
 Subkingdom : Tracheobionta (Vascular plant)
 Super Devisi : Spermatophyta (Generating seeds Plant)
 Devisi : Magnoliophyta (flowering plants)
 Kelas : Magnoliopsida (Dicots)
 Ordo : Malvales
 Famili : Muntingiaceae
 Genus : Muntingia
 Spesies : Muntingia calabura L.

In Indonesia, it is called "Kersen". In some area, it is known *ceri* (Jakarta), *baleci* (Madura). The other names in various country such as: *datiles*, *aratiles*, *manzanitas* (Philippines); *mât sâm* (Vietnamese); *khoom sômz*, *takhôb* (Laos); *takhop farang* (Thailand); *krâkhôb barang* (Cambodia); and *kerukup siam* (Malaysia). *Capulin blanco*, *cacaniqua*, *nigua*, *niguito* (Spain); *Jamaican cherry*, and Singapore *cherry* (England). While old Netherlands called Japanese Cherry.

Chemical Content in Cherry: The chemical contents in cherry are saponins, flavonoids, polyphenols and essential oils. In every 100gr of cherry contain 77, 8 of water, 0,384 of protein, 1,56gr of fat, 17,9gr of carbohydrate, 4,6 of fiber, 1,14gr of ash, 124,6mg of calcium, 84mg of fosfor, 1,18 of iron, 0,019 gr of carotene, 0,065gr of tannine, 0,037gr of riboflavin, 0,554 of niacine and 80,5mg of vitamin C.

Cholesterol: Cholesterol is one of fat compound colored with yellow which is in normal level is very important in various process of metabolism in body, such as to forming cell walls, sex hormone, wrapping neural networks, forming vitamin D for bone, material of forming acids and salts to emulsify the fat, as well as to the development of brain cells of children. But when the level of excess, it can be a problem, because it will clogged arteries, especially in corener artery so it will block blood flow. This situation can increase risk of serious disease such as coronary heart disease and stroke. Cholesterol is the essential structure component to every cell and the main component of brain and nerve cells. Cholesterol

is a high concentration in glandular tissue and in heart where synthesized and stored. Cholesterol is a material among important steroid formation, such as bile acid, folic acid, adrenal cortex hormones, estrogen, androgen and progesterone.

Because of the body is needed so cholesterol continuously shaped or synthesized in liver. Even it is about 70% of cholesterol in blood are syntheses resulting in liver, while 30% is donation of food intake. As long as the amount of good cholesterol synthesized or derived from food is still disproportionate to the needs of the body will remain healthy, but with the development of the lifestyle of the people who tend to consume a lot of fatty foods, the level of cholesterol intake is higher than the level of needs.

The Benefits of Cholesterol in Body: Cholesterol in blood is very needed by body in certain amount because it has three main functions, such as:

- Cholesterol helps form the outer sheath cell.
- Cholesterol helps form bile acids that digest food in the gut.
- Cholesterol allows the body to form vitamin D and hormones, such as estrogen in women and testosterone in men.

The Classification of Lipoprotein: The fat in blood consists of Cholesterol, phospholipids, and free fatty acids. Cholesterol, triglycerides and phospholipids is related with special protein, apoprotein to be lipoprotein complex. This relation cause fat solubility, fused and flows in the bloodstream. While free fatty acid related with albumin. Lipoprotein is divided into 5 main groups.

- Chylomicrons
- Very Low-density lipoprotein (VLDL)
- Intermediate density lipoprotein (IDL)
- Low-density lipoprotein (LDL)
- High-density lipoprotein (HDL)**

Normal level in blood can be seen in table 1 below:

Table 1. Normal Level of Cholesterol in Blood

Name of Cholesterol	Normal Level (mg/dl)	Normal threshold (mg/dl)	High Level (mg/dl)
LDL (<i>Low-density lipoprotein</i>)	<130	130-159	>160
HDL (<i>High-density lipoprotein</i>)	>45	35-45	<35
Total of Cholesterol	<200	200-239	>240

Factors Increasing of Cholesterol Level in Blood:

Food favored, smoking, wrong diet and less in sport or physic activity can cause diseases. The delicious food usually has a high level of fat and one of the effects is high cholesterol. Cholesterol usually is found in food of animal origin, like brain, egg yolk, chicken skin and viscera. However, the foods which contain carbohydrates and saturated fats such as flash, margarine, cheese, palm oil and coconut oil by the liver can be formed into cholesterol and triglycerides.

Elevated cholesterol levels in the blood not only occur in adults or older adults, but also in teenagers especially in family who has high cholesterol. It is also based on lifestyle. Besides the irregular lifestyle, there are other factors such as the risk that cannot be changed and lifestyle factor. The risk that cannot be changed is such as increasing age that causes the increased cholesterol level. Then the gender factor, pre-menopausal women have a lower risk of developing cholesterol than men. But after menopause, cholesterol levels are increased. Lifestyle factors are such as Obesity causes cholesterol levels tend to rise. However, it is possible for that skinny is not necessarily safe from attack high cholesterol.

The Relationship between High Cholesterol, Atherosclerosis, CHD and Stroke:

Atherosclerosis is one of atherosclerosis. Atherosclerosis is the situation marked by loss of elasticity (stiffening) from artery because thickening of the artery wall that will cause degenerative heart disease, stroke and other arterial diseases. Atherosclerosis has a positive correlation (85%) with deaths due to heart disease (cardiovascular), (4). Atherosclerosis is caused by thickening of fatty substances in and under the layer of the artery wall, which also occurs in the coronary arteries (the arteries of the heart). There is a Greek word that means "watery gruel" while sclerosis which means "hardening". Thus, atherosclerosis is the accumulation of fat tissue deposition (atheroma) in the pulse. The deposition of fat is called plaque, consisting mainly of cholesterol and its esters, and tends to occur at the points of branching pulse that disrupts the blood flow is not so heavy (4). If the blockage occurs in the arteries that supply the heart, they can lead to heart attack or angina (pain that indicates that the heart is not getting enough oxygen). If the blockage is located in the brain, a stroke can occur. Cardiovascular disease is affected not only because it automatically pick the high lipid levels. However, the facts show that the higher the levels of LDL (Low density lipoprotein) and lower HDL (high density lipoprotein) the higher the risk of cardiovascular disease.

Handling Blood Cholesterol Levels

There are generally two ways in handling cholesterol:

1. Do some revolutions in lifestyle.

The revolution in lifestyle can help in reducing cholesterol levels and cardiovascular risk such as:

- a. Reduce fat intake
 - b. Emphasis on consumption fruits and vegetables
 - c. Reduce salt intake
 - d. Losing weight if overweight
 - e. Extend physic activity (Regularly)
 - f. Stop smooking
 - g. Avoid alcoholic beverages
2. Cholesterol-lowering drugs

The use of traditional recipes regularly, proper diet and regular exercise for some sufferers has been very helpful uncontrolled blood fats. But if the use of these methods cannot suppress or control blood fats then the last thing you can do is to use drugs that lower blood fats (hippolipidemik).

Currently the market is widely available cholesterol-lowering drugs, with the workings of different. Statin is usually the drug of choice because it shows that in addition to lowering cholesterol levels, this class of drugs may protect the heart in other ways, such as maintaining healthy blood vessel surface.

The Combination between Duck Eggs and Profile Tiourasil on Cholesterol Increasing:

Nearly all of the fats in duck egg are contained in the yolk, reached 35%, while in the white is nothing at all. Fat in the egg consists of triglycerides (neutral fats) phospholipid (generally in the form of lecithin) and cholesterol. Propylthiouracil may bind to proteins. Inside the egg albumin there is one protein, because of the bond between propiltourasil with albumin causes metabolic processes exceeds the synthesis process thus stimulating hipolisis process and the release of free fatty acids. The increase in free fatty acids causes increase levels of cholesterol and triglycerides in the blood (1). Propiltourasil rapidly absorbed, reaching peak levels after one hour. Bioavibilitas by 50% -80% can be caused by imperfect absorbsinya by first-pass big heart. Most of propiltourasil which is in the body is excreted by the kidneys within 24 hours (3).

RESEARCH METHOD

The Materials: Plant materials are leaves of cherry were fresh and were old, carboxyl methyl cellulose (CMC), propylthiouracil, simvastatin, ethanol, sodium chloride, Pb (II) acetate, iron (III) chloride, mercury (II) chloride, potassium iodide, iodine, α -

naphthol, citric acid, bismuth nitrate, ether, chloroform, isopropanol, methanol, anhydrous sodium sulfate, ethyl acetate, magnesium powder, zinc powder, hydrochloric acid, toluene, sulfuric acid, and a duck egg.

Tools: For this research the instruments include: Glass tools, balance of electricity (Mettler Toledo), the balance of animals digital (Tanita), blender (National), a pipette, oral sonde, filter paper, hot plate, tool measuring blood cholesterol levels Nesco® Multicheck, mortars and stamper, a set of distillation equipment for determination of water content (Azeotropi), rat cage, microscopes, glass objects, cover glass, rotavapour (Buchi), freeze dryer (Edwards), percolator.

Stages of labor

- a. The collection of cherry leaves are dried and powdered to powder simplicia, phytochemical screening, and the water content is determined by means azeotropi.
- b. Making perexion
- c. Making extracts, percolation method with 80% ethanol.
- d. Animals induced with egg yolk 80%, 0.125% propylthiouracil each given approximately 4 ml per day for 10 consecutive days until there is an increase in blood cholesterol levels.
- e. Decreased effectiveness test cholesterol levels dar ethanol extract of leaves of cherry, with a comparison to simvastatin

Intake and Preparation of Animal Experiments

Animals used were male rats weighing 200-300 grams, with 5-8 months of age as much as 30 individuals, obtained by direct purchase at the pet-Feedings pellet. After two weeks, the experimental animals are used for research

Testing the effectiveness of the decline in cholesterol levels: Male rat that had been prepared for the experiments conditioned for one week before testing was conducted. Then it is fasted for 18 hours prior to the tests yet to be given a drink. On the day of testing, the initial cholesterol levels checked each mouse by using a measuring device, Nesco® Multicheck blood cholesterol levels, blood was collected from the mice. Then it is induced with egg yolk 80%, 0.125% propylthiouracil each given approximately 4 ml per day for 10 consecutive days.

After 10 days the mice is tested by cholesterol levels, and then divided into five groups each group consisting of 6 animals, namely:

1. Group 1: as a blank CMC suspension by as much as 4 ml of 0.5%
2. Group 2: as a comparison given simvastatin 0.025% by 4 ml
3. Group 3: supplied with suspension cherry leaf extract 2% 2 ml
4. Group 4: given the suspension of cherry leaf extract 4% 2 ml
5. Group 5: supplied with suspension cherry leaf extract 6% 2 ml

Each animal was given the test substances induced cholesterol appropriate treatment groups. Then check the cholesterol levels is done by the time interval 24 hours until a white rat cholesterol levels return to normal as early before the induced yolk and propylthiouracil.

The obtained data were statistically tested by ANOVA (analysis of variants) and LSD (least Significant Difference).

THE RESULT OF RESEARCH

Screening results phytochemicals: Results of phytochemical screening showed class of chemical compounds contained in the leaves of cherry fresh, simplicia leaf cherry, and the ethanol extract of leaves of cherry is the same that class of alkaloids, flavonoids, steroids, essential oils and tannins, means no damage materials during the manufacturing process simplisia and extracts. The presence of the chemical content of the compound, especially flavonoids, alkaloids, and tannins is potentially cherry leaf ethanol extract has the ability to lower cholesterol

The Effectiveness Test Results Decreased cholesterol levels: Based on the data it can be seen that the percentage decrease in cholesterol levels in the blood faster rats at doses of extract with a concentration of 4% and 6%, compared with a concentration of 2%. This shows that the ethanol extract of cherry leaf can lower blood cholesterol levels because it looks increasingly higher doses of ethanol extract of leaves of cherry suspension is given, the greater the effect of decreasing blood cholesterol levels in the rats tested.

Table 2. Cholesterol Reduction Observations

% Level Blood Cholesterol Reduction					
Time	Control (CMC)	Extract 2%	Extract 4%	Extract 4%	Comparison (Symvastatine)
1 st Day	1.54 ± 0.14	27.48 ± 0.49	49.72 ± 0.99	51.01 ± 0.59	58.54 ± 1.02
3 rd Day	4.10 ± 0.97	37.17 ± 0.64	66.92 ± 0.85	70.98 ± 0.78	70.98 ± 0.96
5 th Day	9.00 ± 0.97	42.94 ± 0.88	81.36 ± 1.07	81.37 ± 0.97	91.71 ± 1.18
7 th Day	19.78 ± 0.95	59.18 ± 0.80	90.19 ± 0.15	90.29 ± 1.27	100.0 ± 0.00
9 th Day	38.06 ± 1.17	83.26 ± 0.95	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00
11 th Day	49.90 ± 1.26	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00
13 th Day	68.93 ± 1.45	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00
15 th Day	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00	100.0 ± 0.00

Table 2 above shows that there are differences in the percentage of reduction in blood cholesterol levels; animals given ethanol extract of leaves of cherry suspension with various concentrations. The data which is obtained from the testing of anti-hypercholesterolemic is continued testing statistically using ANOVA one way to see whether there is any difference in the effect of decreasing cholesterol levels significantly among all groups of animals treated with the test materials with differences in various concentrations, then if there are differences continued test LSD (least significant difference) to see whether there is a significant difference between the test material with one another (2). The results of ANOVA test can be seen in Table 3 as follows:

Table 3. Result of ANOVA Test

Day	F0	F-table	
		5%	1%
3 rd	16.361	2,76	4,18
7 th	25.771	2,76	4,18
11 th	25.811	2,76	4,18
13 th	7.452	2,76	4,18
15 th	0,16	2,76	4,18

Table 3 above shows that started from 3rd day until 13th day, except for 15th day, the price obtained F₀ is greater than F-table, the percent reduction in blood cholesterol animals is differ significantly from one another. Hence continued LSD test results are in Table 4 below.

Table 4. The Result of BNT Test

Time	Treatment	% KT Reduction	CMC	Simvastatine	2% Extract	4% Extract
1 st Day	CMC	1.54	-	-	-	-
	Simvastatine	58.54	57	-	-	-
	2% Extract	27.48	25.93	31.06	-	-
	4% Extract	49.72	48.18	8.82	22.24	-
	6% Extract	51.01	49.47	7.53	23.54	1.29
BNT_{0.05} = 0.214 BNT_{0.01} = 0.291						
3 rd Day	CMC	4.1	-	-	-	-
	Simvastatine	70.98	66.87	-	-	-
	EEDM 2%	37.17	33.07	33.8	-	-
	EEDM 4%	66.92	62.82	4.05	29.75	-
	EEDM 6%	67.59	63.49	3.38	30.42	0.67
BNT_{0.05} = 0.268 BNT_{0.01} = 0.363						
7 th Day	CMC	19.87	-	-	-	-
	Simvastatine	100	80.22	-	-	-
	Extract 2%	59.18	39.4	40.82	-	-
	Extract 4%	90.18	70.41	9.81	31.01	-
	Extract 6%	90.29	70.51	9.71	31.12	0.11
BNT_{0.05} = 0.245 BNT_{0.01} = 0.331						
11 th Day	CMC	49.9	-	-	-	-
	Simvastatine	100	50.1	-	-	-
	Extract 2%	100	50.1	0	-	-
	Extract 4%	100	50.1	0	0	-
	Extract 6%	100	50.1	0	0	0
BNT_{0.05} = 0.166 BNT_{0.01} = 0.225						

Seen in Table 4 that the first to the third day there were very significant differences between the test materials extract various concentrations, blank (CMC) and the comparator (Simvastatin). The eleventh day there was no difference between the comparator (Simvastatin) with various concentrations of extracts of the test material.

Overall it can be seen that the ethanol extract of leaves of cherry has activity to lower blood cholesterol levels of animals tested, for their real differences with the group form (CMC) is% reduction in cholesterol levels of the group given the test material extract is very large if it compared with a group of animals blank (CMC). Judging from various extract concentration seen that the effectiveness of the extract with a concentration of 4% is very good for a reduction in blood cholesterol levels, because on the seventh day did not differ significantly with the concentration of 6%.

CONCLUSION

The results of the preliminary investigation of chemical constituents of fresh leaves, powder simplicia and cherry leaf ethanol extract (*Muntingia calabura* I) Containing compound glycosides, flavonoids, steroid / triterpenoida and tannins. Cherry leaf extract (*Muntingia calabura* I) Can lower blood cholesterol levels. The concentration of 4% to give a very good effect as the seventh day did not differ significantly by 6% each given 2 ml, although they still differ significantly with simvastatin 0.025% by 4 ml. Ethanol extract of leaves of cherry has been shown to have efficacy decrease in cholesterol levels, so it can be developed into drugs cholesterol-lowering alternatives from natural materials, for this needs to do further research, include toxicity tests, and test product development, including clinical trials on volunteers, so it will get medicine reduction in cholesterol levels from natural materials which rational, easy to obtain, easy to use with relatively minor side effects.

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