Glycation, Glycation inhibitors and Wellaging

H·E·A·T

H.E.A.T. International Congress on Anti-Aging Medicine
September 13-14, 2019

Dr Serge Ginter
Luxembourg

Wellaging

Risks

- CV Diseases
- cancer risk
- dementia
- osteoporosis
- exogenous risks: accidents, suicides ...

Prevention

Optimization

- Metformin
- Inositol
- Aspirine
- Melatonine……..

Aging

- progressive accumulation of molecular damage caused by environmental and metabolically generated free radicals,
- by spontaneous errors in biochemical reactions, and by nutritional components
- cellular dysfunction,
- reduced stress tolerance, diseases and ultimate death.

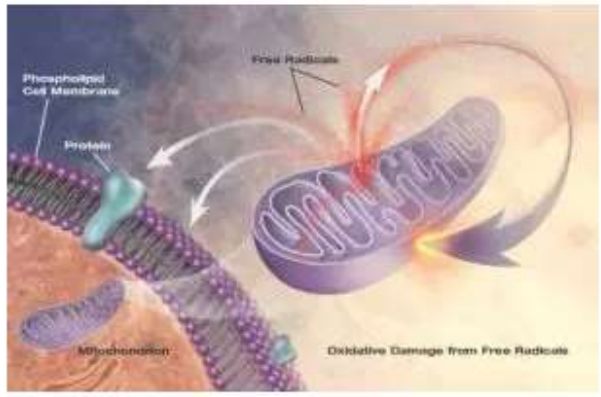
Journal of Free Radical Research, Volume 40, 2006 - Issue 12
Theories of biological aging: Genes, proteins, and free radicals
Suresh I.S. Rattan

MarioFit – Healthy Tips – The 4 Major Health Destroyers: Oxidation, Inflammation, Glycation, Abnormal Methylation

mariofit1 / November 6, 2013

Health Destroyers? Sounds like a war. And indeed there is a warfare inside our bodies. Experts in the field of genetics and longevity identified the 4 major aging markers that slowly kill our cells and promote a faster degeneration of our body. If we act to take control of any of these aging markers, we can slow the path of aging and reduce greatly our chances of developing the 21st century diseases – including cancer, heart and cardiovascular diseases, diabetes and obesity.

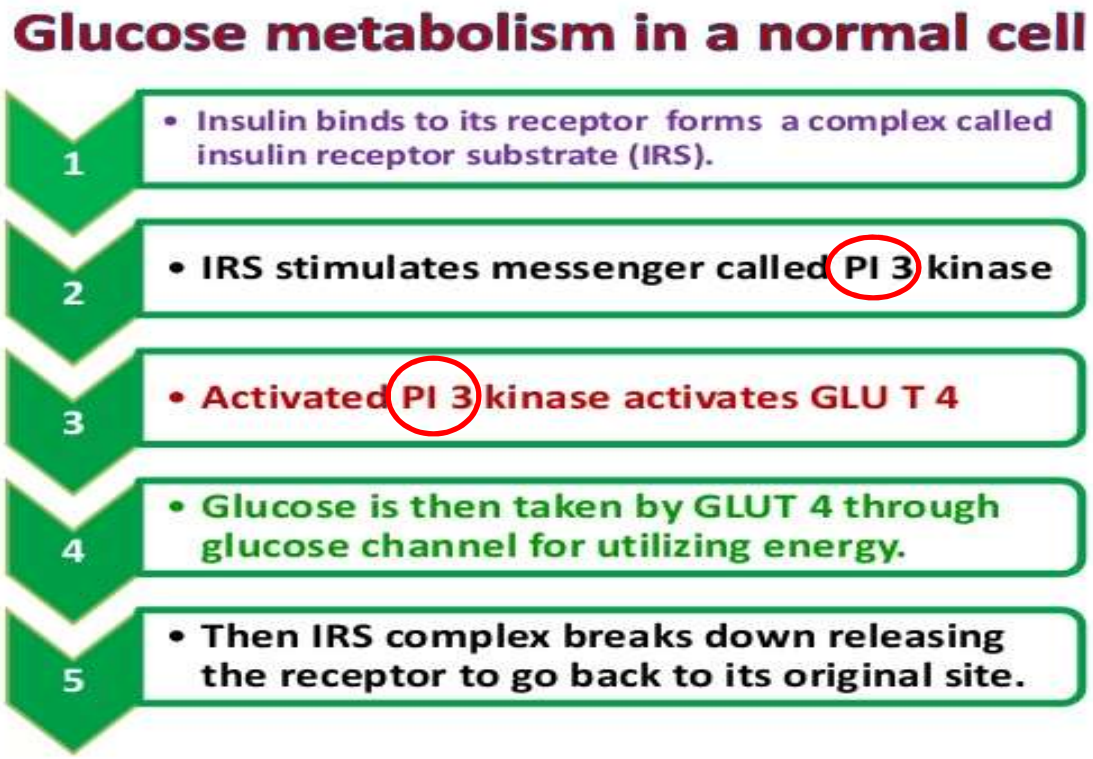
Below is a brief description of these 4 health destroyers and what might be a better solution to fight against them. A more detailed explanation you will find it on my website: www.mariofit.ca



OXIDATION. Oxygen is essential for life. But when exposure to pollution, stress, unhealthy foods or too much physical exercise, free radicals are created overwhelming the body's limits to detoxify. Those free radicals are mostly chemically unstable reactive molecules of oxygen that are involved in breaking of bonds between other molecules.

In normal unpolluted environment, controlled production of free radicals in the body might help protecting us from some microbes and viruses. But in excess, those free radicals create an excessive oxidative stress, which attack all living molecules and cellular membrane, destroying the cells, lowering the immune system and promoting premature aging. It is like rusting inside our body that creating many degenerative diseases such as cancer, stroke, myocardial infarction, diabetes and others.

Glucose Metabolism



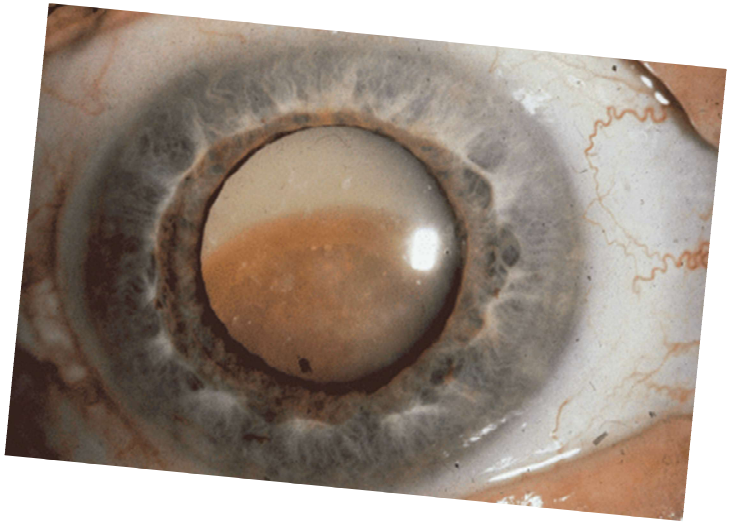
The Maillard-Reaction

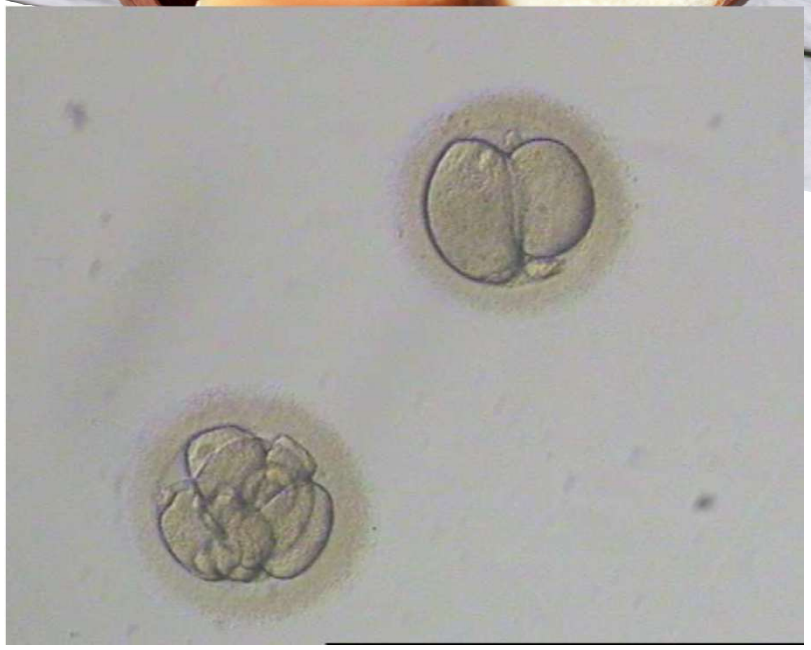
-The Maillard reaction is a chemical reaction between amino acids and reducing sugars that gives browned food its distinctive flavor.

-The reaction is a form of non-enzymatic browning which typically proceeds rapidly from around 140 to 165 °C.

-At higher temperatures, caramelization and subsequently pyrolysis become more pronounced and potential carcinogen called acrylamide can be formed.

Maillard-Browning





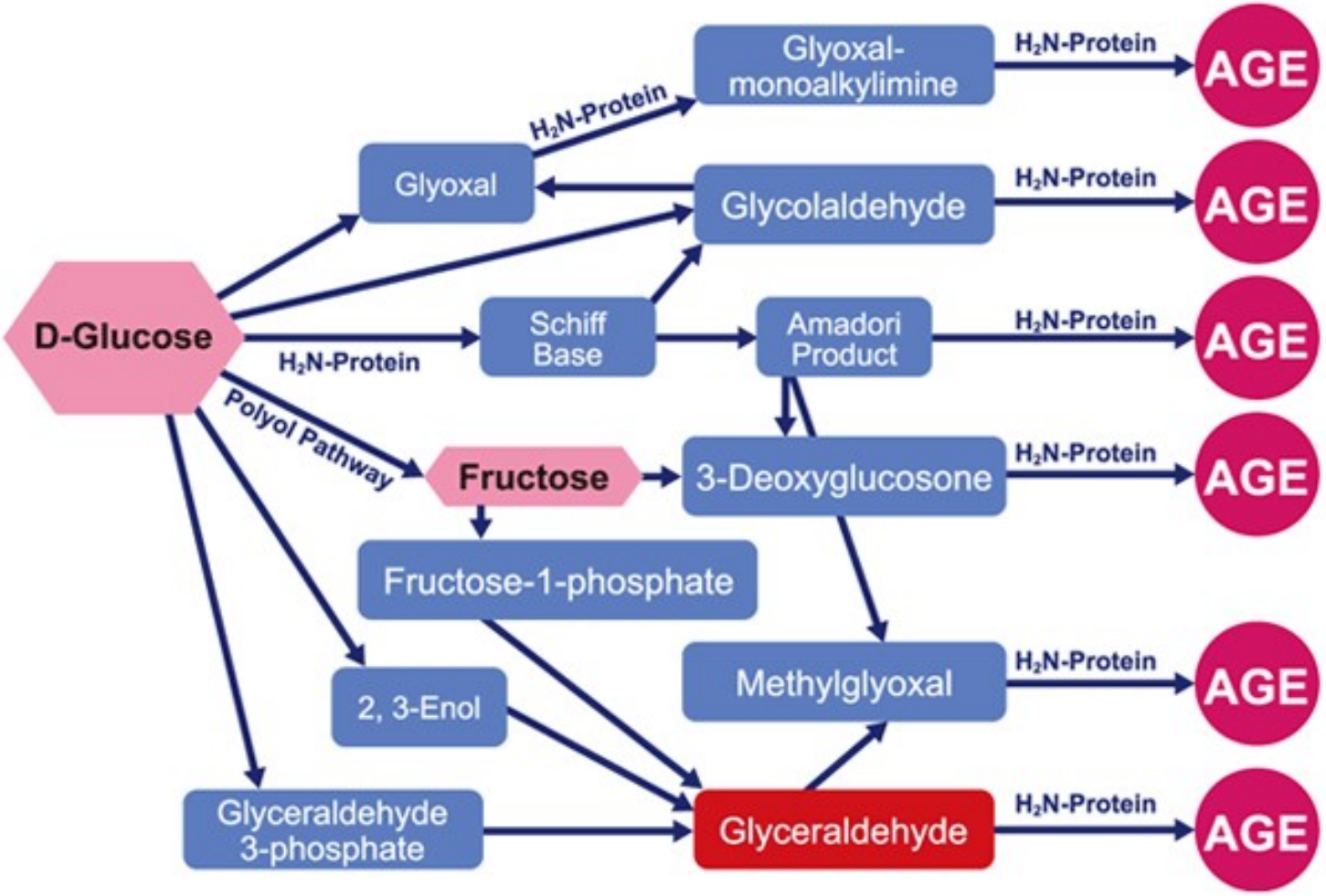
Glycation is also in food products

- Acrylamide
- Benzopyrenes
- Heterocyclic amines






Glycation

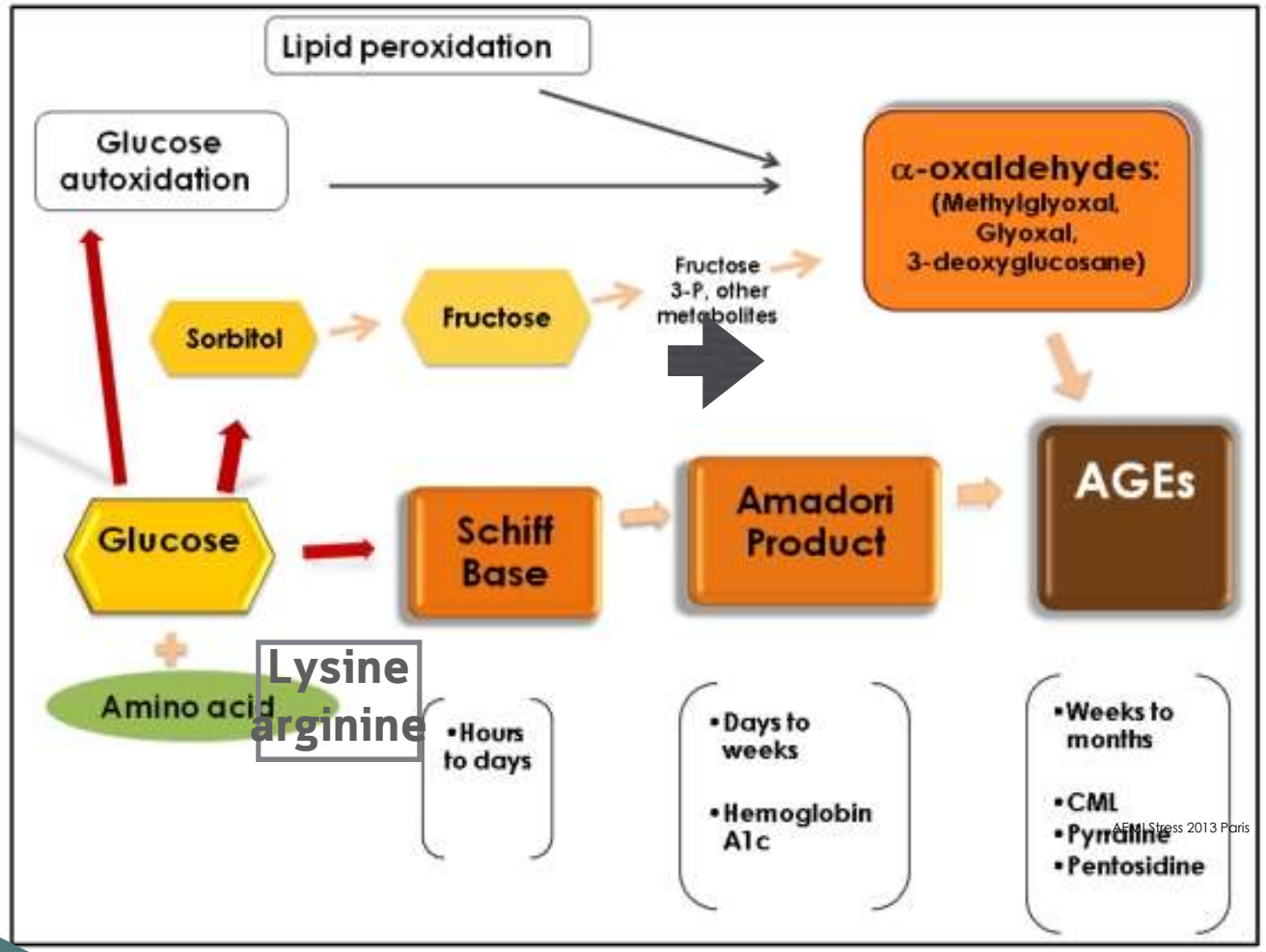

D-Glucose
H₂N-Protein
Schiff Base
Amadori Product
H₂N-Protein
AGE
Polyol Pathway
Fructose
3-Deoxyglucosone
H₂N-Protein
AGE
Fructose-1-phosphate
Glyoxal
H₂N-Protein
Glyoxal-monoalkylimine
H₂N-Protein
AGE
Glycolaldehyde
H₂N-Protein
AGE
2, 3-Enol
Methylglyoxal
H₂N-Protein
AGE
Glyceraldehyde 3-phosphate
Glyceraldehyde
H₂N-Protein
AGE

Heterogeneity of AGE

Glyoxale, Glycolaldehyde, Methylglyoxal , z.B.

- Carboxymethyl-Lysin (CML)
- Carboxymethyl-l-Arginin (CMA)
- Glyoxal-Lysin-dimer (GOLD)
- Methyl-glyoxal-Lysin-dimer (MOLD)
- Glyceraldehyde pyridinium-typ (GLAP)
- Pyrraline
- 3-DG-Imidazolone
- etc….

What's Glycation ➡ Oxydativ Stress

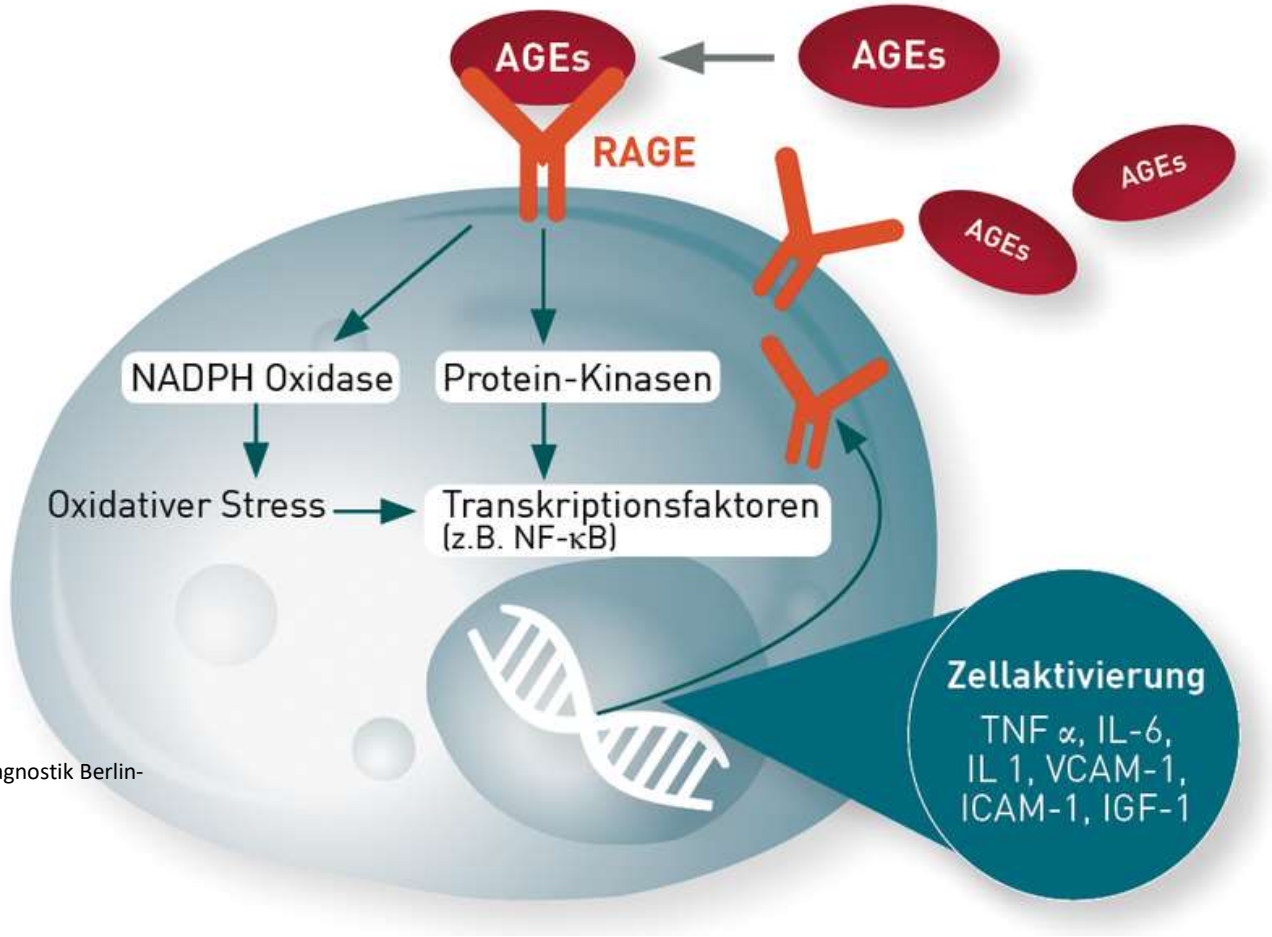


Proteins
Lipids
DNA
RNA
Hormones

Advanced Glycation Endproducts (AGE) consequences

- oxidative stress
- hyperglycemia
- decreased leptin (reduces hypothalamic stimulation)
- hypertension via renin-angiotensin activation
- vascular damage
- AGE are inflammatory
- AGE worsen angiogenesis
- circulatory disorder
- higher cancer risk (perpetuated cell activation)
- higher dementia risk

Cellular transcription of AGEs?



Institut für Medizinische Diagnostik Berlin-Potsdam MVZ GbR

Advanced Glycation Endproducts (AGE) consequences on fertility

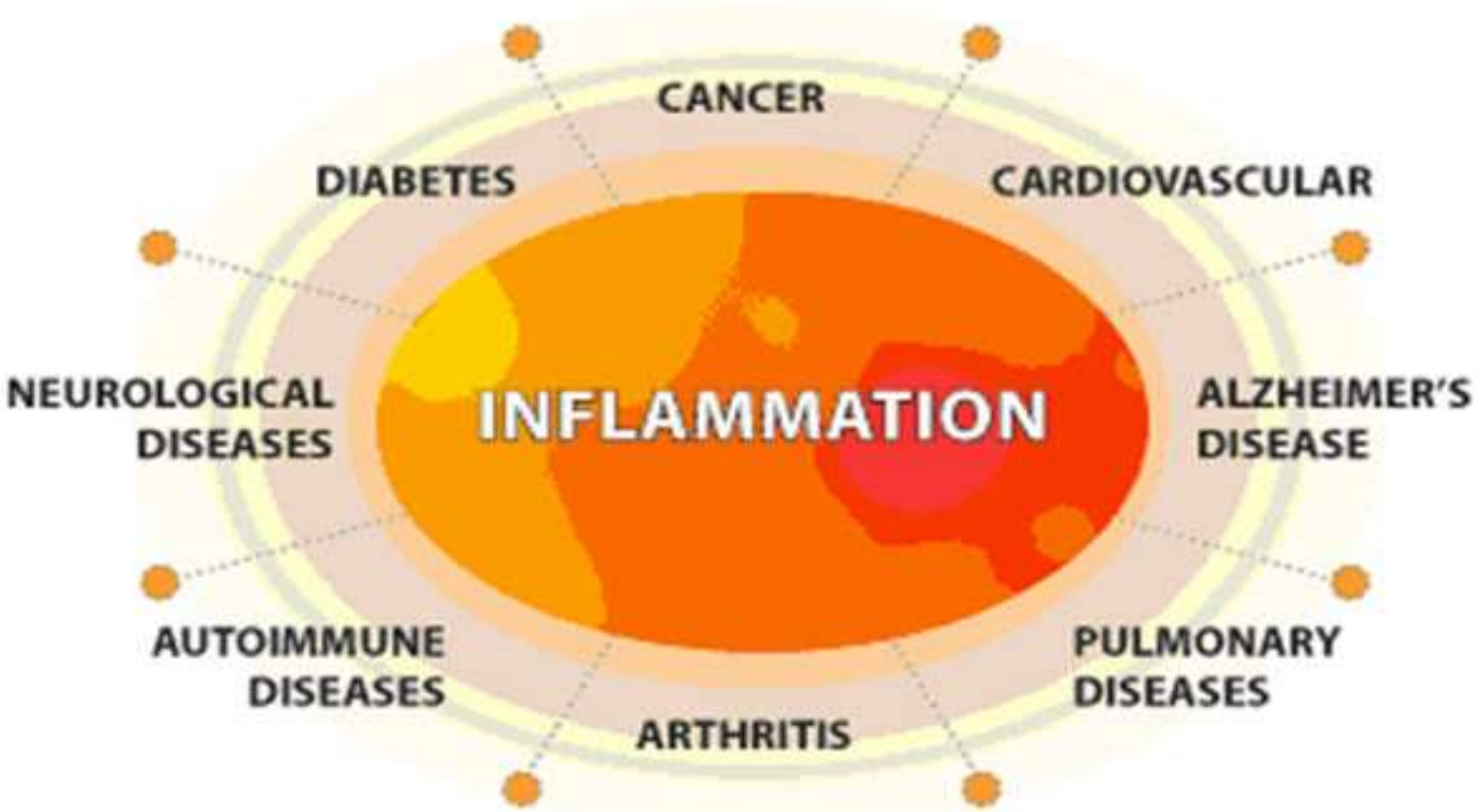
- Glycans alter the zona pellucida
- Testosterone rises
- Estrogen drops
- Ovulation rate drops
- Fertilization rate drops
- Endometrial receptivity decreases
- Pregnancy rate drops
- Abortion rate is rising

AGEs and literature

- **Accumulation of advanced glycation end products of the Maillard reaction with age in human hippocampal neurons** Takemi Kimur, a, Junichi Takamatsua, Kazuyoshi Ikedab, Akira Kondoc, Taihei Miyakawad, Seikoh Horiuchib
- **Photo-Enhanced Modification of Human Skin Elastin in Actinic Elastosis by N∈-(Carboxymethyl)lysine, One of the Glycoxidation Products of the Maillard Reaction**
- Kumiko Mizutari 1, Tomomichi Ono 1, Kazuyoshi Ikeda 2, Ken-ichi Kayashima 1, Seikoh Horiuchi 2
- **Role of the Maillard Reaction in Aging of Tissue Proteins**
- ADVANCED GLYCATION END PRODUCT-DEPENDENT INCREASE IN IMIDAZOLIUM CROSS-LINKS IN HUMAN LENS PROTEINS*
- Elisabeth Brinkmann Frye‡, Thorsten P. Degenhardt‡, Suzanne R. Thorpe‡,§ and John W. Baynes‡,§¶
- **Age-related accumulation of Maillard reaction products in human articular cartilage collagen**
- N Verzijl, J DeGroot, E Oldehinkel, SR THORPE… - Biochemical …, 2000 - biochemj.org
- **Inhibitors of the Maillard reaction and AGE breakers as therapeutics for multiple diseases**
- VP Reddy, A Beyaz - Drug discovery today, 2006 – Elsevier
- **Angiogenic Effects of Advanced Glycation End Products of the Maillard Reaction on Cultured Human Umbilical Cord Vein Endothelial Cells** M. Tezuka, N. Koyama, N. Morisaki, Y. Saito, S. Yoshida, N. Araki, S. Horiuchi
- **Inhibitors of Advanced Glycation End Product Formation and Neurovascular Dysfunction in** Experimental DiabetesAnnals of the New York Academy of Sciences, June 2005,Volume 1043, The Maillard Reaction: Chemistry at the Interface of Nutrition, Aging, and Disease, Pages 784–792
- **Advanced glycation end-products accumulation compromises embryonic development and achievement of pregnancy by assisted reproductive technology** Masao Jinno1,*, Masayoshi Takeuchi2, Aiko Watanabe1, Koji Teruya3, Jun Hirohama1, Noriko Eguchi1 and Aiko Miyazaki4

Atherosclerosis - An Inflammatory Disease

(Russell Ross,
N Engl J Med 1999)


CANCER
DIABETES
CARDIOVASCULAR
NEUROLOGICAL DISEASES
INFLAMMATION
ALZHEIMER'S DISEASE
AUTOIMMUNE DISEASES
PULMONARY DISEASES
ARTHRITIS

Measurements of AGE

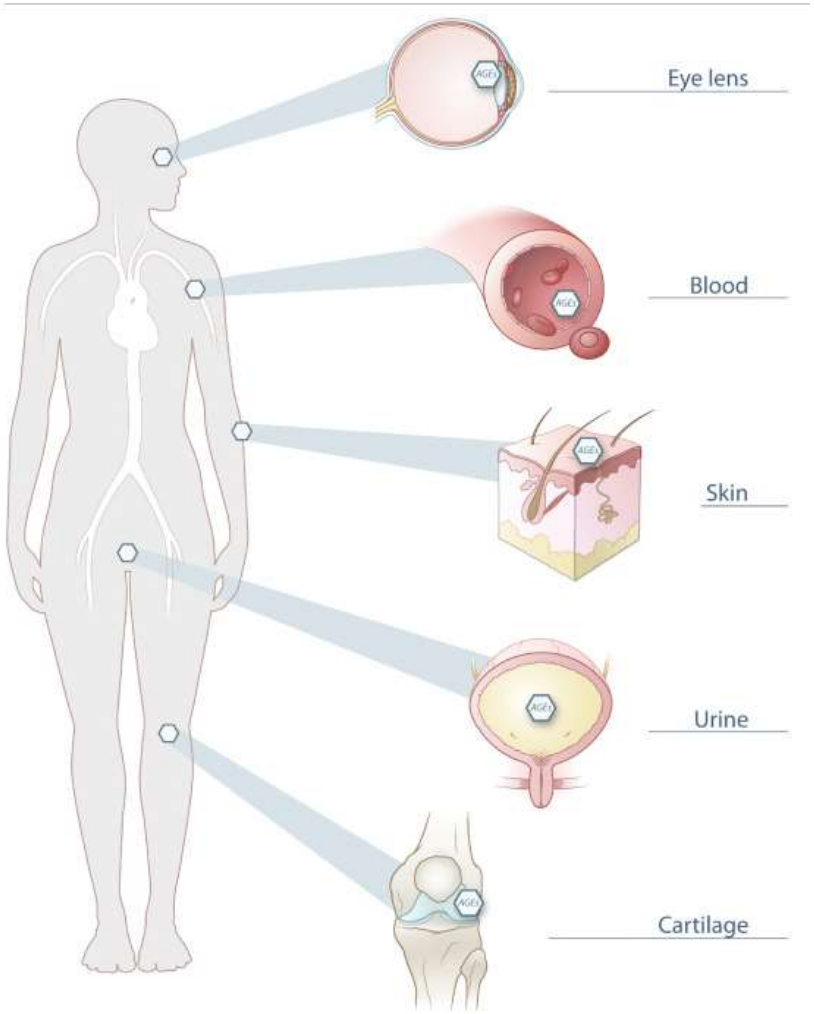


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Fig. 2. Measurements of advanced glycation end products (AGEs).

Skin autofluorescence (SAF)

- An emerging biomarker is advanced glycation end products (AGEs).
- AGEs are strongly associated with peripheral artery disease (PAD).
- Skin autofluorescence (SAF) is a noninvasive method to assess skin AGEs.
- SAF identifies PAD patients at highest risk for local and cardiovascular end points.

HbA1c

A close relation between the amounts of red cell HbA1c and Hb-AGE

Therapeutics which Inhibit the Accumulation of AGEs

AGE Formation Inhibitors

aminoguanidine metformin, Aspirin has demonstrated the capacity to decrease AGE accumulation

angiotensin-converting enzyme (ACE) inhibitors have the added benefit of reducing AGE accumulation

The benefits of vitamin B compounds like Pyridoxamine, a vitamin B6 derivative, prevents the formation of AGEs from Amadori intermediates Thiamine and Benfotiamine are liposoluble derivatives of vitamin B1 which also exhibit AGE-lowering properties

Carnosine is a naturally occurring dipeptide which is known to exist in the brain as well as many other tissues. Importantly, it has a number of activities which aid in the reduction of AGE accumulation.

Cleavage of Pre-Formed AGEs

Novel therapeutics such as N-phenacylthiazolium bromide (N-PTB) and alagebrium chloride cleave cross-links

Blockade of Cellular Receptors of AGEs

Binding of AGEs to proteins such as the receptor for advanced glycation end products (RAGE)

Thiazolidinediones (TZDs) have recently been identified as RAGE antagonists

Inhibitors of Advanced Glycation End Products (AGEs)

Guanidines

- **AG (Aminoguanidine) (Pimagedine)**
- **Metformin**

Pyridoxamine (PM) est l'une des formes de la vitamine B6, avec la pyridoxine et le pyridoxal.

Atorvastatin (Lipitor)

Kremezin

Inhibitors of Renin-Angiotensin System (RAS)

Inositol

Aspirin

Carnosine

Acarbose

The best cross-link inhibitors currently available are
-carnosine, aminoguanidine, metformin and acarbose

No cross-link breakers are commercially obtainable as yet, but these will be marketed within 2-3 years.

Soon after, combinations of inhibitors and breakers are due to follow.

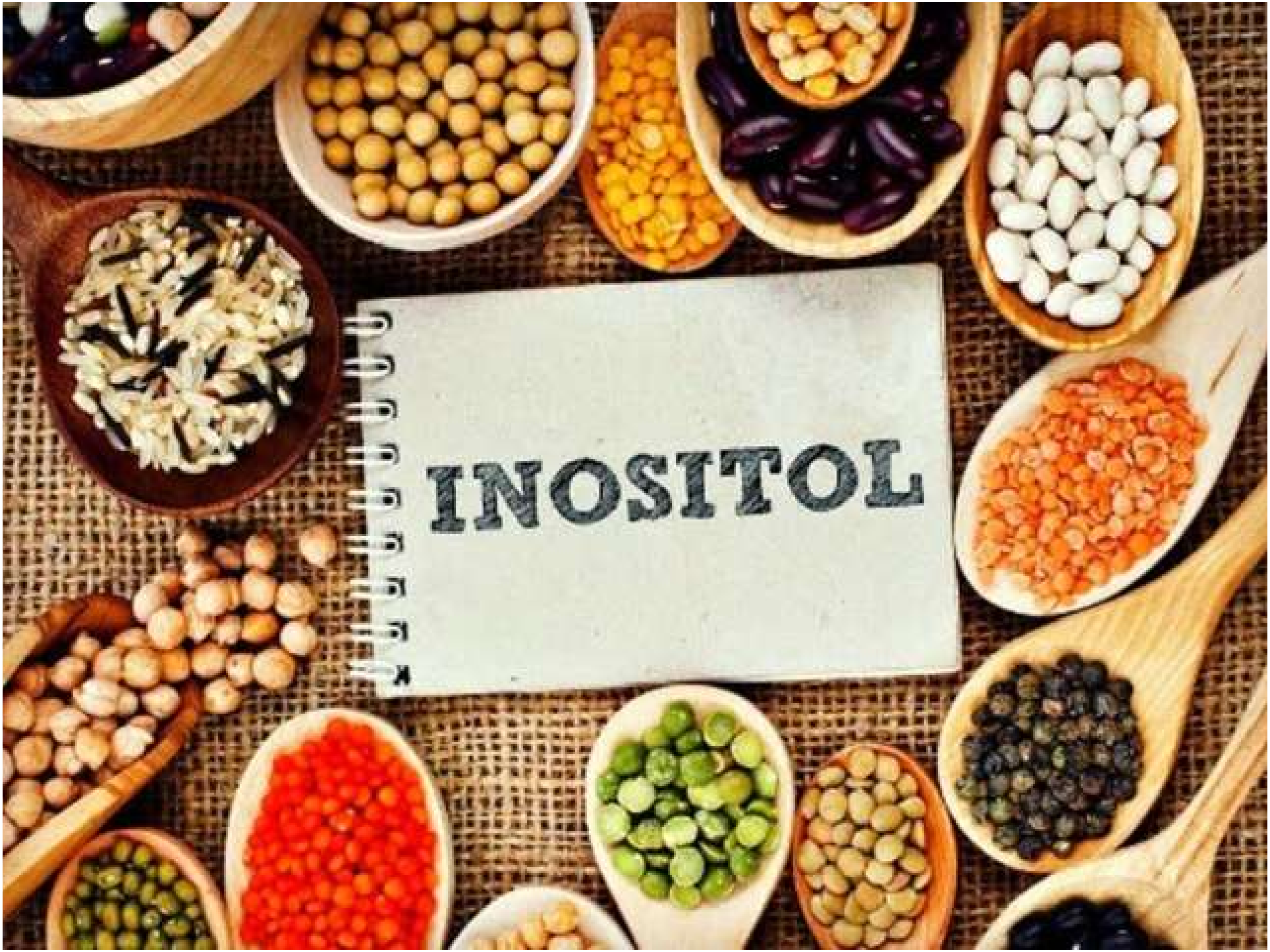
Kremezin

AST-120 (Kremezin; Kureha Chemical Industry Co Ltd, Tokyo, Japan) is an orally administered adsorbent showing adsorption for certain organic compounds known to be precursors of substances that accumulate in patients with chronic kidney disease (CKD)

Inhibitors of Renin-Angiotensin System (RAS)

Cardiovasc Hematol Agents Med Chem. 2007 Oct;5(4):249-64.
Inhibition of renin-angiotensin system and advanced glycation end products formation: a promising therapeutic approach targeting on cardiovascular diseases.
Geronikaki A1, Gavalas A, Dislian V, Giannoglou G.
Author information
Abstract
Cardiovascular disease remains the leading cause of death worldwide. The renin-angiotensin-aldosterone system (RAAS) plays a key role in the regulation of blood pressure, through the actions of angiotensin (Ang) II. Excessive RAAS activity may lead to hypertension and associated target organ damage. Indeed, RAAS blockade with angiotensin converting enzyme inhibitors (ACEIs) and/or angiotensin receptor AT (1) blockers (ARBs) has proved to be successful treatment for arterial hypertension, heart failure and diabetes. Accumulating evidence suggests that arterial stiffness is an important and independent predictor of cardiovascular risk. More recently, a role for advanced glycation end-products (AGEs) in the development of arterial stiffening has been suggested. Advanced glycation end-products form by a nonenzymatic reaction between reducing sugars and biological proteins. Mechanisms underlying these alterations include AGE cross-linking of collagen and AGE interactions with circulating proteins and AGE receptors. New pharmacologic agents that prevent AGE formation, break cross-links, or block AGE receptors reduce vascular and myocardial stiffness, inhibit atherosclerotic plaque formation, and improve endothelial function. These agents promise to reduce the risk of isolated systolic hypertension, diastolic dysfunction, diabetes and thus, heart failure.

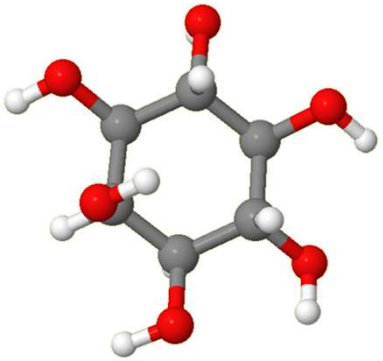
PMID: 17979687

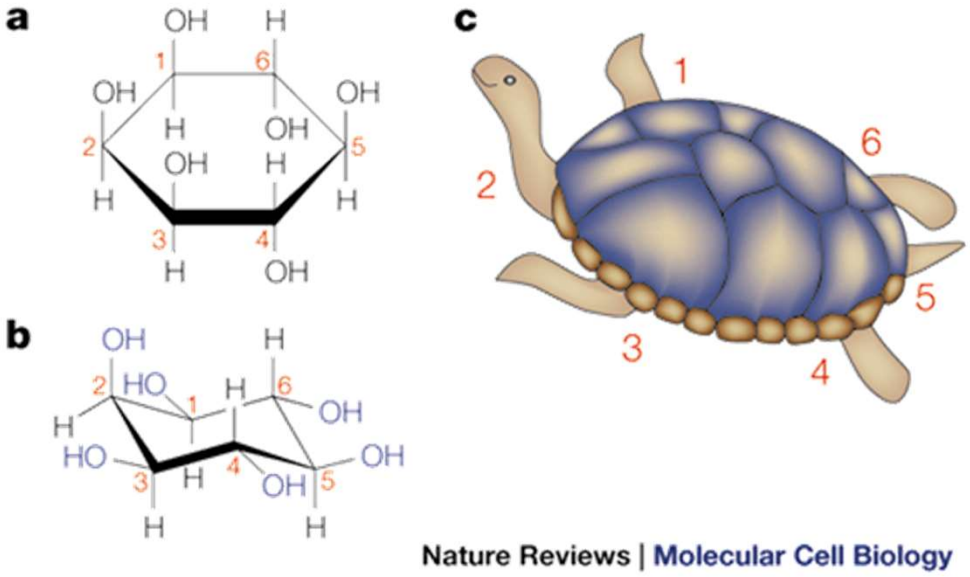

INOSITOL

Inositols and AGE

***In vitro* studies indicated that IP6 significantly reduced the formation of fluorescent AGEs**

INOSITOLS



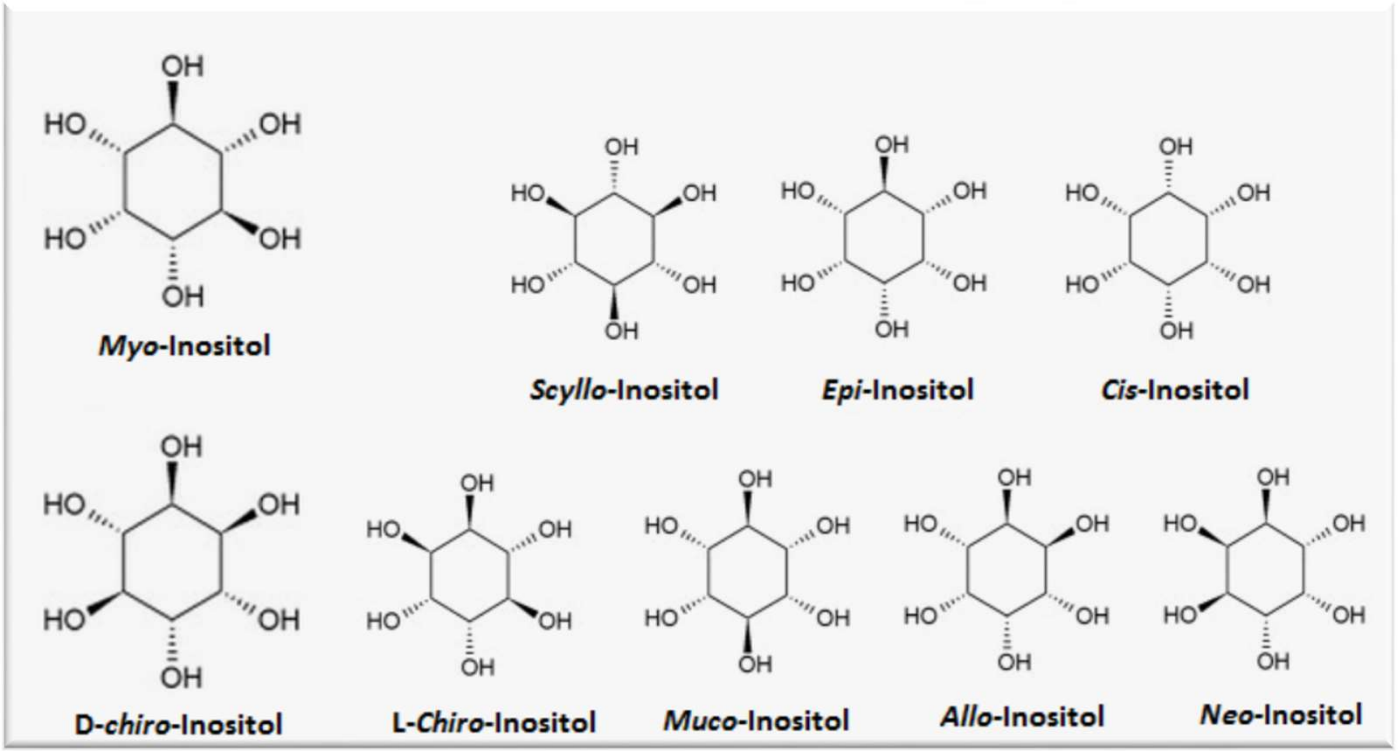


Inositol is a 6-carbon, cyclic polyalcohol wrongly considered as belonging to the group of vitamins B

It exists in nine different stereoisomers

Robin F. Irvine, Back in the water: the return of the inositol phosphates. Nature Reviews Molecular Cell Biology (May 2001)

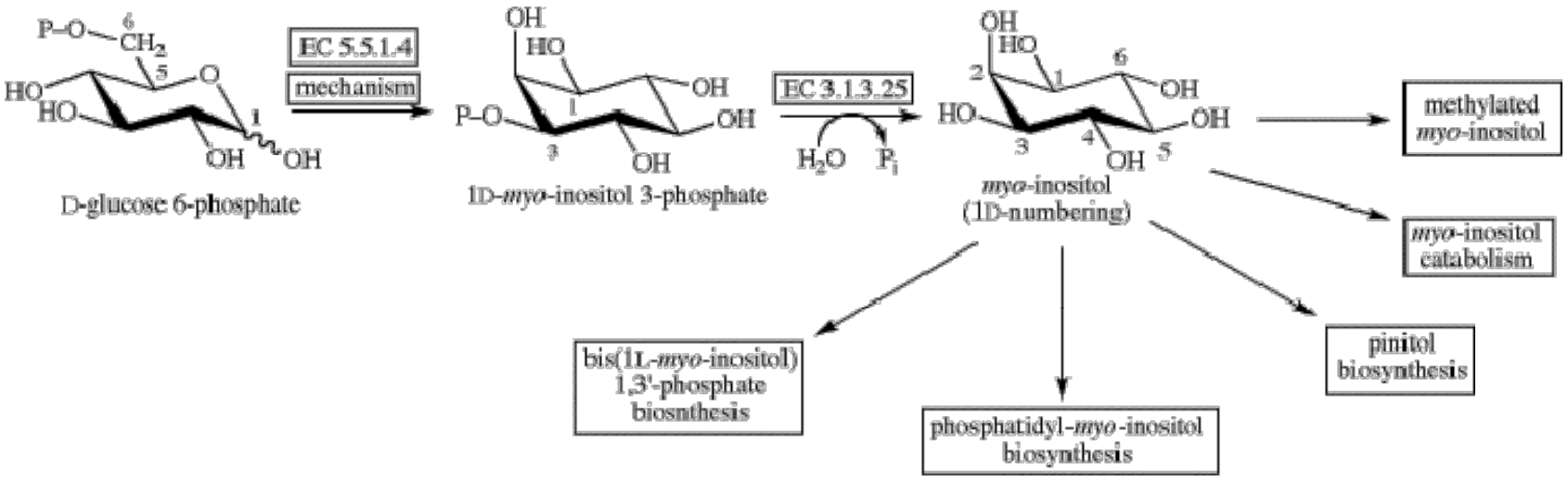
Inositol's isomers



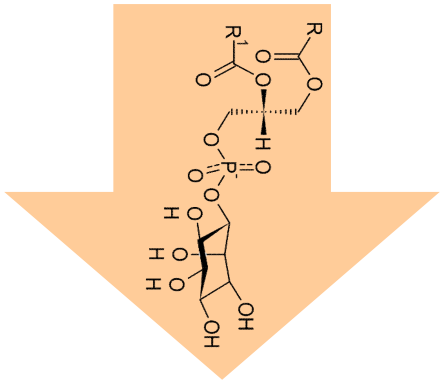
Myo-inositol is the most abundant in nature

Inositol and Diet

It is also an endogenous molecule directly synthetized by adrenal gland



Inositols form

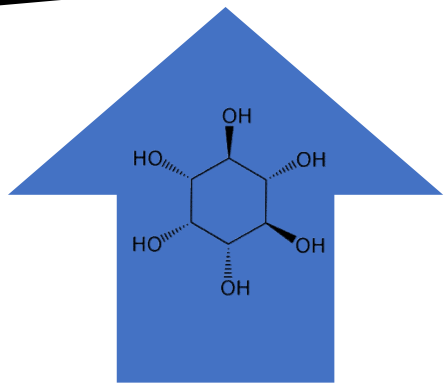


Inositol complexes

(abundant in cell membranes)

Free inositol

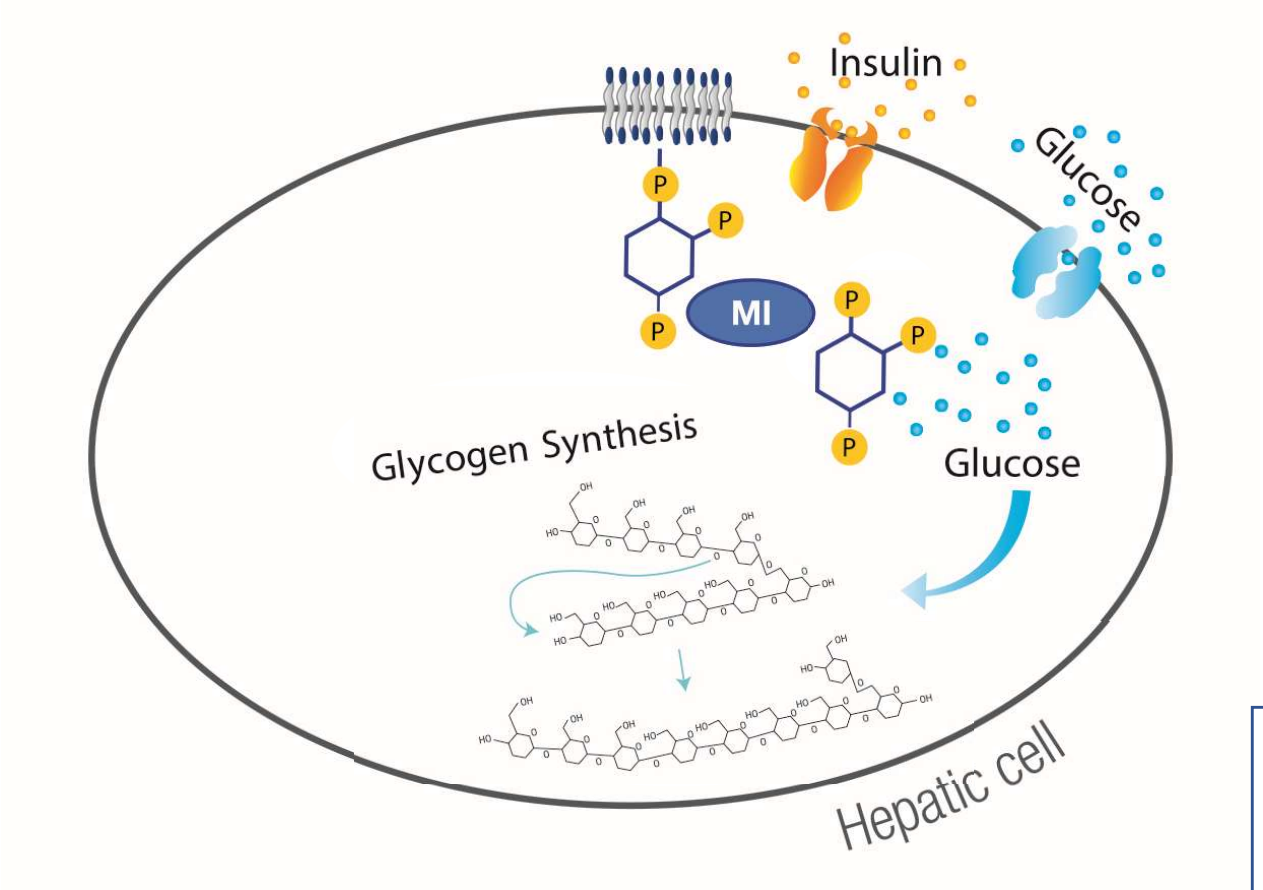
(abundant in body fluids)



Myo-Inositol Beneftits

MI & Insulin

MI improves the insulin signaling reducing glycaemia



Glucose in the bloodstream

Insulin in the bloodstream

Other functions

CELL SURVIVAL and GROWTH

Essential for the growth and survival of cells (Eagle et al, 1956)

MOOD

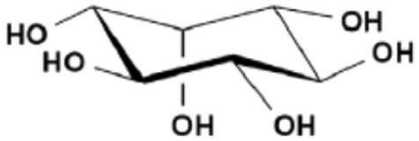
Proposed selective serotonin reuptake inhibitor-like role (Gianfranco et al, 2011)

CENTRAL NERVOUS SYSTEM

MI is essential for the development and function of peripheral nerves (Chau et al, 2005)

REPRODUCTION

Restores normal ovulatory activity (Unfer et al, 2012)
↑ Oocyte and egg quality (Ciotta et al, 2011 – Unfer et al, 2011)
↑ Fertilization rate
↑ sperm motility and mitochondrial membrane potential in vitro (Condorelli et al, 2012 et 2011)



myo-inositol

OSTEOGENESIS

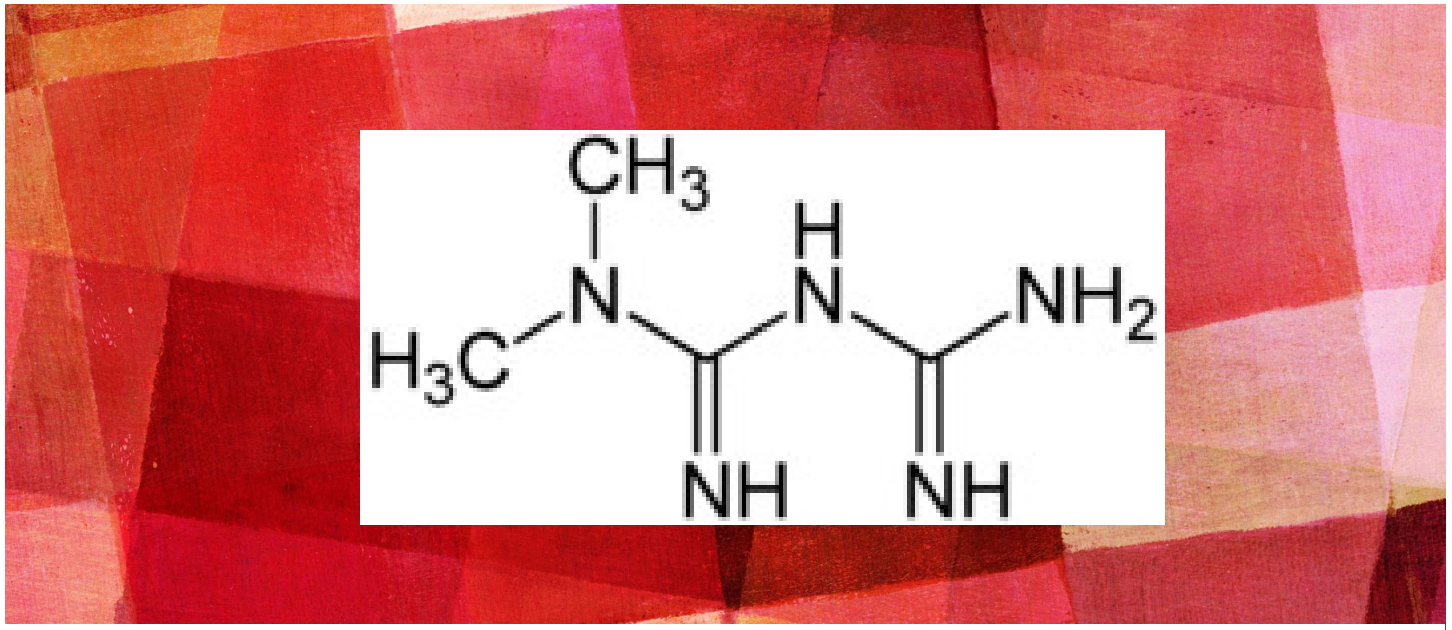
↑ Calcium in bone
↑ strength of bone structure
MI is essential to bone formation, osteogenesis and bone mineral density (Dai et al, 2011)

METABOLISM

↑Insulin Sensitivity
(↓HOMA-IR, ↓Glycemia, ↓insulinemia)
↓Total and LDL-cholesterol
↑ HDL-cholesterol
↓ Serum Triglycerides
(Unfer et al, 2012 – Santamaria et al, 2012 – Croze et al, 2012 - Maeba et al, 2008 – Ortmeyer et al, 1996)

Marine L. Croze, Potential role and therapeutic interests of myo-inositol in metabolic diseases. Biochimie 2013


Inositol
Myo-Inositol
Miovarian
NosiFol-D
MYOFD
Myo-Inositol Powder
OVASITOL
Oocyt Plus
INOFOLIC
Myceed
Pregnitude
MYO-INOSITOL
D-CHIRO-INOSITOL
SOLAL
D-Chiro-Inositol with Manganese Sulfate
Chirosital
D-chiro-inositol, Vitamin D3 Tablets
Myo-Inositol, D-chiro-inositol, chromium & Vitamin D3 Tablets
Noxis
DCI
Cystaheal
Ovlary
Supplement Facts
Serving Size : 2 Capsules
Servings Per Container: 30
Amount per Serving
%DV
Chiro Inositol
200mg
Myo inositol
500mg
Chaste Tree
300mg
† Daily Value (DV) not established



i-methyl biguanid

METFORMIN

the geroprotector

Metformin in Longevity Study (MILES)

This study is ongoing, but not recruiting participants.

Sponsor:
Albert Einstein College of Medicine, Inc.

ClinicalTrials.gov Identifier:
NCT02432287

First Posted: May 4, 2015
Last Update Posted: June 27, 2017

Information provided by (Responsible Party):
Jill Crandall, Albert Einstein College of Medicine, Inc.

Purpose

Metformin, an FDA approved first-line drug for the treatment of type 2 diabetes, has known beneficial effects on glucose metabolism. Evidence from animal models and in vitro studies suggest that in addition to its effects on glucose metabolism, metformin may influence metabolic and cellular processes associated with the development of age-related conditions, such as inflammation, oxidative damage, diminished autophagy, cell senescence and apoptosis. As such, metformin is of particular interest in clinical translational research in aging since it may influence fundamental aging factors that underlie multiple age-related conditions. The investigators therefore propose a pilot study to examine the effect of metformin treatment on the biology of aging in humans. Namely, whether treatment with metformin will restore the gene expression profile of older adults with impaired glucose tolerance (IGT) to that of young healthy subjects.

METFORMIN - CARDIOPROTECTIVE EFFECTS

Improves	Decreases
diastolic function	↓ hyperglycemia
↑ HDL-C	↓ TC, VLDL, LDL-C
↑ vascular relaxation	↓ oxidative stress
↑ tPA activity	↓ PAI-1 levels
	↓ von Willebrand factor levels
	↓ platelet aggregation and adhesion

Ann Intern Med 2002;137:25-33

Metformin inhibition of glycation processes

P Beisswenger[1], D Ruggiero-Lopez[2]

SUMMARY

A number of studies have shown that metformin is beneficial in reducing diabetes associated vascular risk beyond the benefits expected from its anti-hyperglycaemic effect. One of the main pathogenic mechanisms leading to chronic complications of diabetes is non-enzymatic glycation where damage is mediated through increased production of highly chemically reactive glucose and α-dicarbonyl compounds which lead to production of advanced glycation products (AGEs). We present laboratory and clinical data supporting the hypothesis that one important explanation of metformin's effect on diabetic complications could be its ability to reduce toxic dicarbonyls and AGEs. This effect could be related either to the binding of the α-dicarbonyls, methylglyoxal (MG) or 3-deoxyglucosone, or to an increase in enzymatic detoxification. Our studies presented in this manuscript document extracellular binding of MG by metformin to form a specific product (triazepinone) *in vivo*. This condensation product appears to be only one of several inactive end products resulting from this chemical reaction and we discuss the possibility that these or other condensation products (hydroimidazolones) could be indicative of inactivation of MG by metformin. Additional studies of other possible condensation products, as well as other potential cellular effects of metformin on MG production, will help to clarify this potentially important effect of metformin and provide a further rationale for using metformin to prevent long-term complications.

Key-words: Metformin · Glycation · Methylglyoxal · Diabetic complications · Triazepinone.

P Beisswenger, D Ruggiero-Lopez. Metformin inhibition of glycation processes.
Diabetes Metab 2003,29,6S95-6S103

Biochemical Pharmacology, Vol. 58, pp. 1765–1773, 1999.

ISSN 0006-2952/99/$–see front matter
PII S0006-2952(99)00263-4

Reaction of Metformin with Dicarbonyl Compounds. Possible Implication in the Inhibition of Advanced Glycation End Product Formation

Daniel Ruggiero-Lopez,‡ Marc Lecomte,* Gérard Moinet,† Gérard Patereau,† Michel Lagarde* and Nicolas Wiernsperger**

*Diabetic Microangiopathy Research Unit, lipha-inserm u352, insa-Lyon, Villeurbanne; and †lipha s.a., Chilly Mazarin, France

ABSTRACT. Dicarbonyl compounds such as methylglyoxal and glyoxal are extremely reactive glycating agents involved in the formation of advanced glycation end products (AGEs), which in turn are associated with diabetic vascular complications. Guanidino compounds such as aminoguanidine appear to inhibit AGE formation by reacting with α-dicarbonyl compounds. The aim of this work was to study whether the antihyperglycemic agent metformin (a guanidine-like compound) might react with reactive α-dicarbonyls. Metformin was incubated at pH 7.4 and 37° in the presence of either methylglyoxal or glyoxal and reaction products analysed by HPLC coupled to mass tandem spectrometry. AGE formation on albumin by methylglyoxal and glyoxal in the presence or absence of metformin was also studied by measuring the fluorescence at 370/440 nm after albumin–AGE isolation by ultrafiltration. As a standard for mass spectra analysis, a metformin–methylglyoxal adduct was chemically synthesised and characterised as a triazepinone (2-amino-4-(dimethyl-amino)-7-methyl-5,7-dihydro-6*H*-[1,3,5]triazepin-6-one). The results obtained showed that metformin strongly reacted with methylglyoxal and glyoxal, forming original guanidine–dicarbonyl adducts. Reaction kinetic studies as well as mass fragmentation spectra of the reaction products were compatible with the presence of triazepinone derivatives. In the presence of metformin, AGE-related fluorescence after albumin incubation with either glyoxal or methylglyoxal was decreased by 37% and 45%, respectively. These results suggest that besides its known antihyperglycemic effect, metformin could also decrease AGE formation by reacting with α-dicarbonyl compounds. This is relevant to a potential clinical use of metformin in the prevention of diabetic complications by inhibition of carbonyl stress. BIOCHEM PHARMACOL **58**;11:1765–1773, 1999. © 1999 Elsevier Science Inc.

KEY WORDS. advanced glycation end products; carbonyl stress; dicarbonyl compounds; glycoxidation; metformin; triazepin

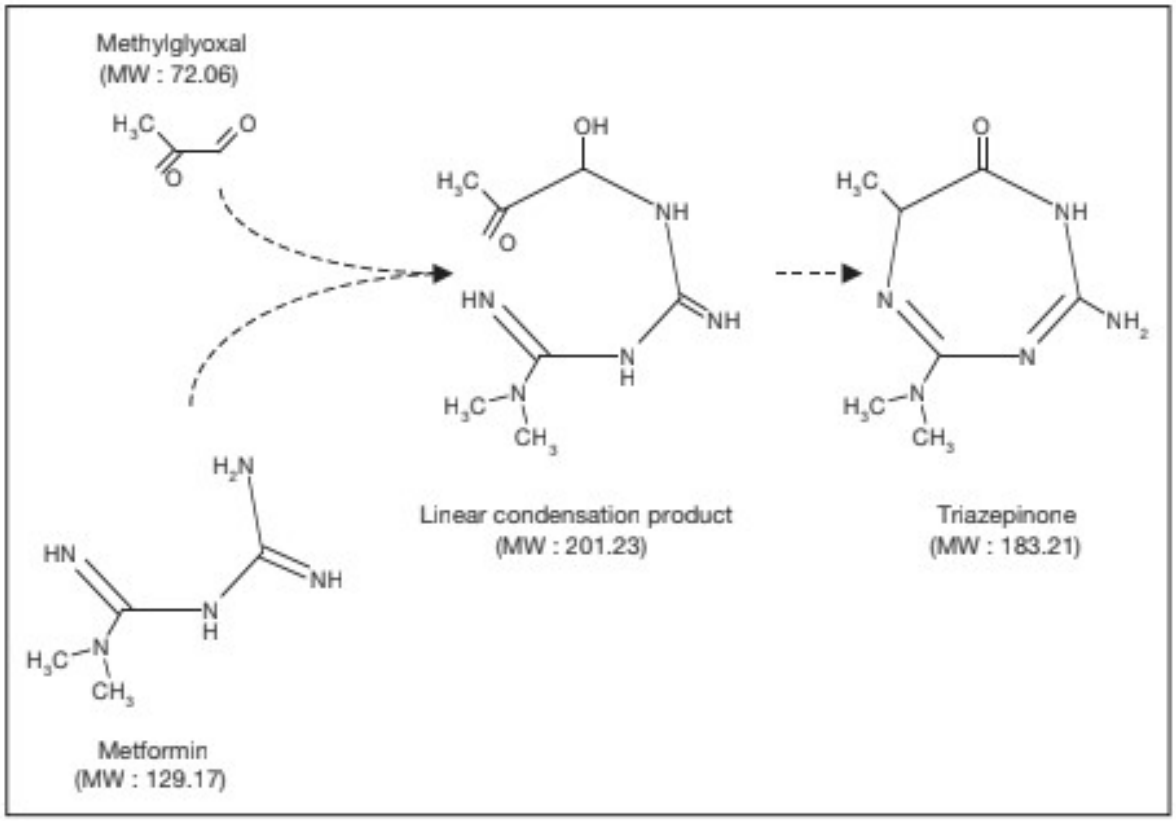


Figure 3
Metformin reaction with methylglyoxal: triazepinone synthesis.

Diabetes Metab 2003,29,6S95-6S103

met down regulate inflammation
&
oxidative stress

level normalisation of :

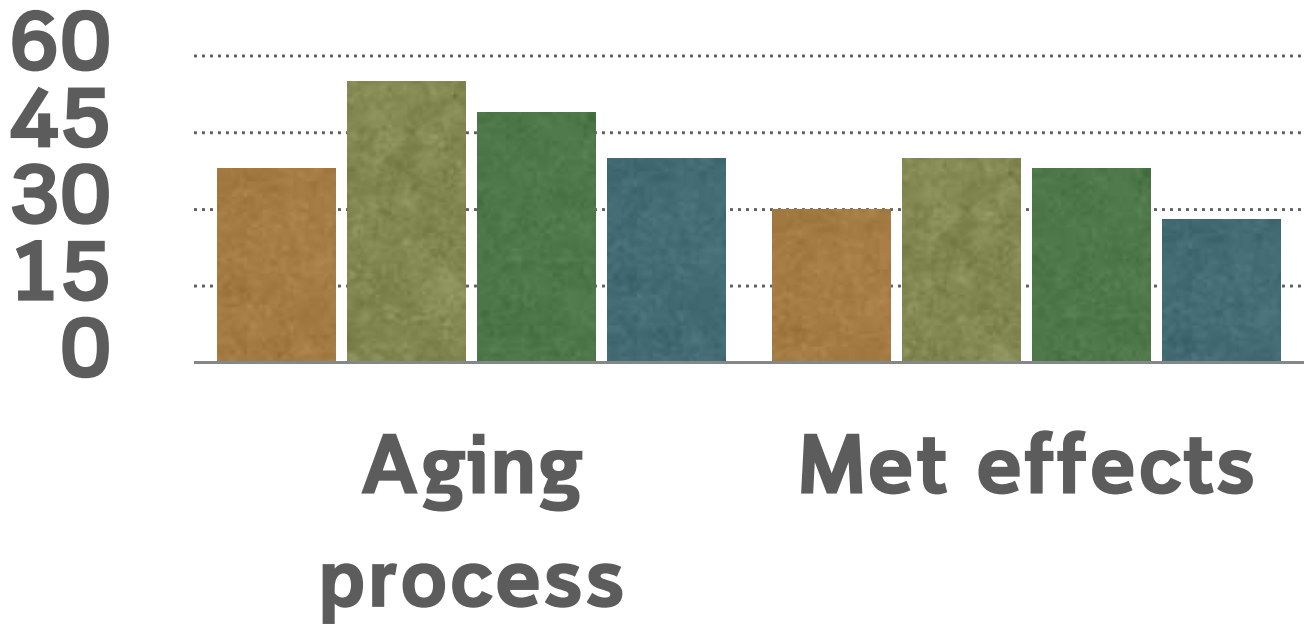
myeloperoxydase
glutathione
catalase
peroxydase

metformin reduces vascular permeability and cellular infiltration

Protective Effect of Metformin against Acute Inflammation and Oxidative Stress in Rat.
Pandey A, et al. Drug Dev Res. 2016.

metformin acts on the major pillards of aging

metformin reduces blood sugar and works on multiple pathways involved in cell growth, inflammation and metabolism — all of which constitute the major pillars of aging.



caloric restriction mimetic

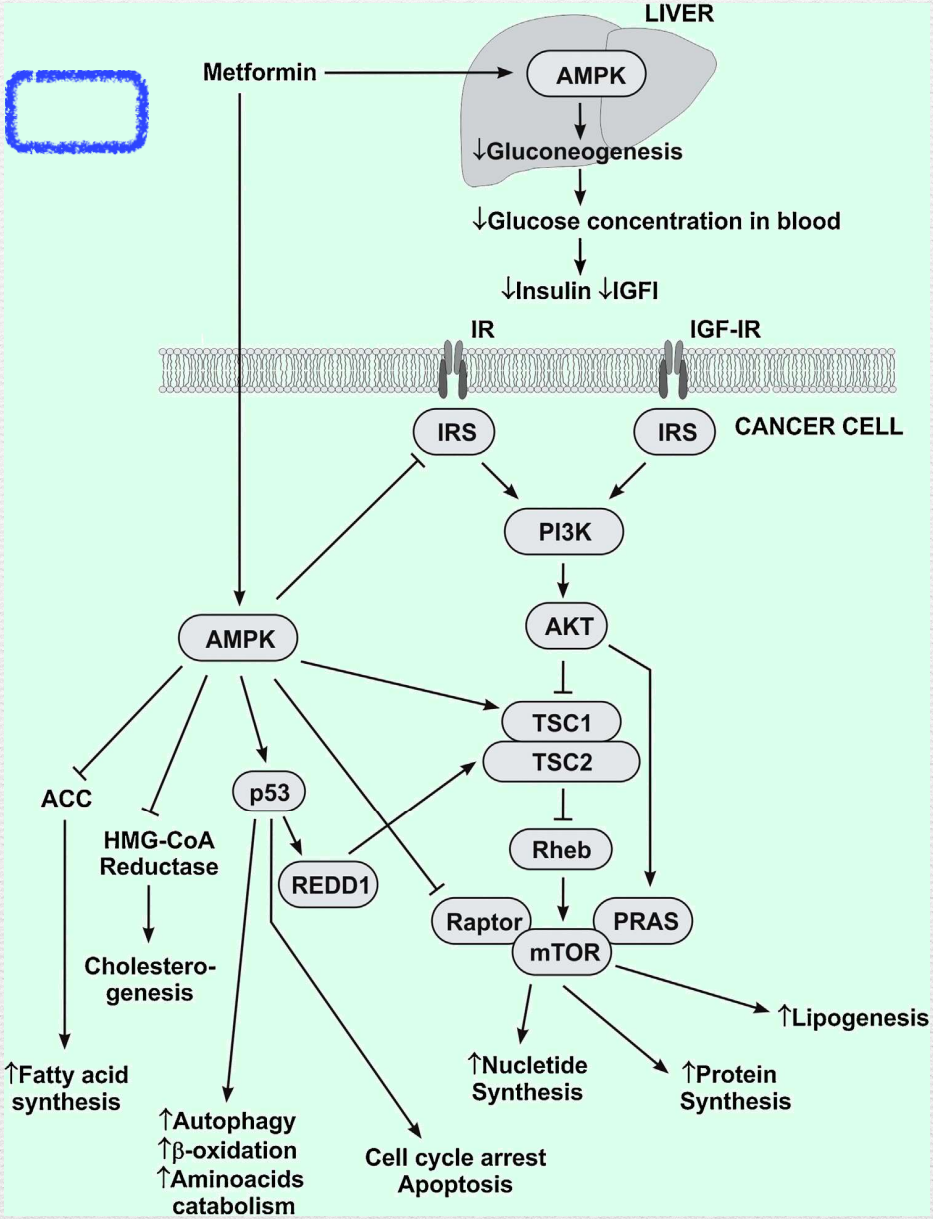
anti insulin/igf1

AMPK

P53

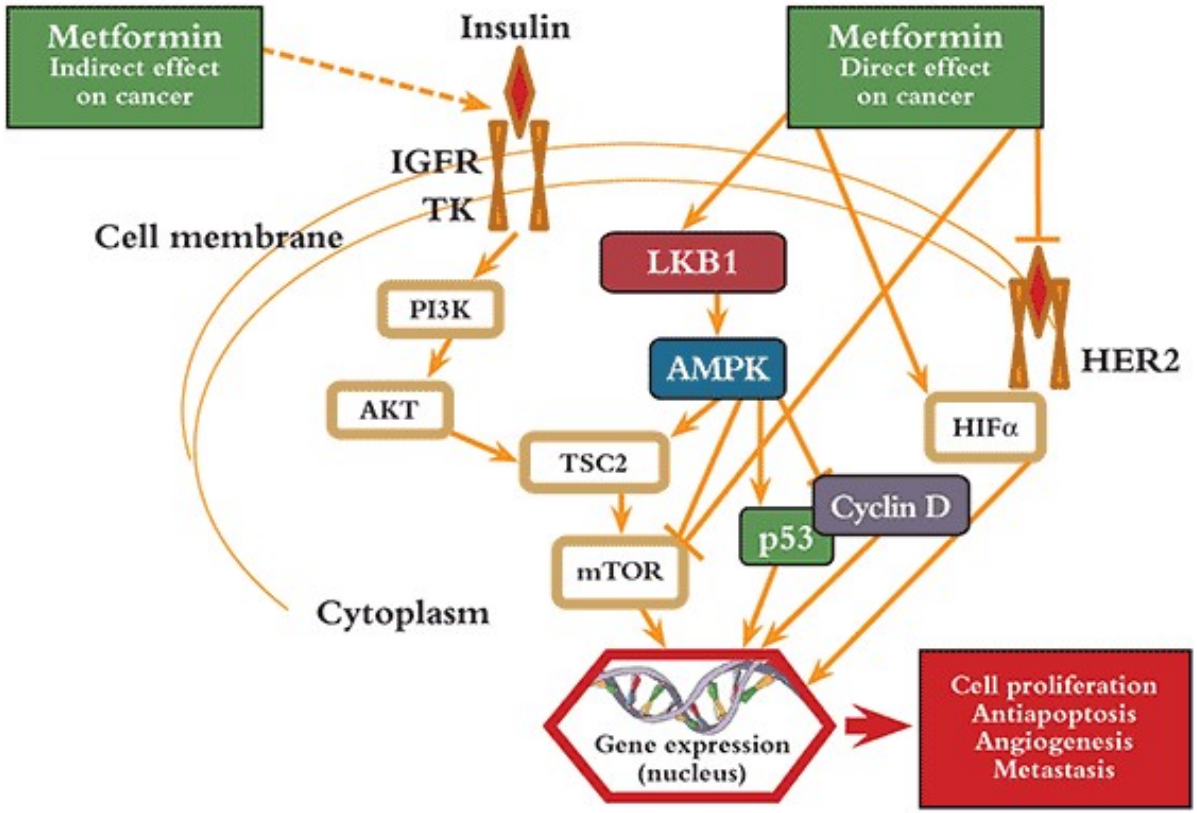
autophagy

apoptose



Metformin induces degradation of mTOR protein in breast cancer cells

Figure 1. Major Potential Antitumor Mechanisms of Metformin



AKT: v-akt murine viral oncogene; AMPK: 5' adenosine monophosphate-activated protein kinase; HER2: human epidermal growth factor receptor 2; HIFα: hypoxia-induced factor alpha; IGFR: insulin-like growth factor receptor; LKB1: serine-threonine liver kinase B1; mTOR: mammalian target of rapamycin; p53: tumor suppressor protein; PI3K: phosphoinositide 3-kinase; TK: tyrosine kinase; TSC2: tuberous sclerosis complex 2.

Metformin induces degradation of mTOR protein in breast cancer cells
Mohamed Alalem, Alpana Ray & Bimal K. Ray

Anticancer Drugs

Aspirin

Other antiinflammatory drugs (?)

statins

metformin

Vitamine D

Hormones: E2, Progesterone, Testosterone, Melatonin

bisphosphonates

denosumab

metformin
&
cancer prevention

Metformin for cancer and aging prevention : is it a time to make the long story short ?

"The problem with metformin ?

is it's cheap, it's widely available, it has a great safety profile, and anyone can use it"

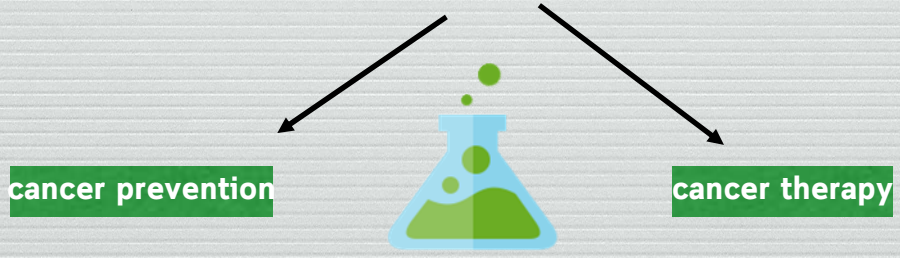
Metformin for cancer and aging prevention: is it a time to make the long story short?

Vladimir N. Anisimov[1] Oncotarget, Vol. 6, No. 37

November 18, 2015

Blagosklonny MV. Validation of anti-aging drugs by treating age-related diseases. Aging (Albany NY) 2009;28;1(3):281-8.

Metformin, an old drug, brings a new era to cancer therapy.



Metformin, an old drug, brings a new era to cancer therapy.
Review article
He H, et al. Cancer J. 2015 Mar-Apr.

in vivo the metformin's role in attenuating tumorigenesis

Aspirin

Diabetes Res Clin Pract. 2007 Aug;77(2):337-40. Epub 2007 Mar 26.

Aspirin inhibits the formation of pentosidine, a cross-linking advanced glycation end product, in collagen.

Urios P, Grigorova-Borsos AM, Sternberg M.

Abstract

Aspirin showed an inhibitory effect on the formation of pentosidine, a cross-linking advanced glycation endproduct, in collagen incubated with glucose in vitro. IC(50) was evaluated at 10mmol/l. Aspirin might act by metallic ion chelating (as did EDTA and DTPA) and by oxygen radical scavenging. Since aspirin was reported to inhibit retinopathy in diabetic dogs, it could act partly by inhibiting advanced glycation endproduct accumulation in long-lived proteins like collagens.

Aspirin Stimulates Insulin and Glucagon Secretion and Increases Glucose Tolerance in Normal and Diabetic Subjects

Piero Micossi, MD, Antonio E Pontiroli, MD, Steven H Baron, MD, Raul C Tamayo, MD, Frieda Lengel, Maurizio Bevilacqua, MD, Umberto Raggi, MD, Guido Norbiato, MD and Piero P Foà, MD,PhD

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Diabetes 1978 Dec; 27(12): 1196-1204. https://doi.org/10.2337/diab.27.12.1196

Previous Next

Aspirin and AGE

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Antidiabetic Antiglycation Drug ?

- The activation of AMPK (AMP-activated protein kinase) also leads to an increase in fat burning and decomposition of fat in the liver. ***(S. Galic et al., Hematopoietic AMPK β1 prevents inflammation and hepatic insulin resistance in obesity. Journal of Clinical Investigation. 2011;121:4903-15)***
- Salicylates activity on AMPK could counteract a diabetic condition. Indeed, there is evidence of an effect in type 2 diabetes mellitus ***(Warum Ass und Metformin vor Krebs schützen. Meyer, Rüdiger in Dtsch Arztebl 2012; 109(17): A-840 / B-724 / C-720).***

Vitamin D and AGE

Mol Cell Endocrinol. 2019 Jan 5;479:87-92. doi: 10.1016/j.mce.2018.09.004. Epub 2018 Sep 22.

Vitamin D attenuates the effect of advanced glycation end products on anti-Mullerian hormone signaling.

Merhi Z[1].

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Fertility and Sterility.

asrm American Society for Reproductive Medicine

Vitamin D attenuates the adverse effect of advanced glycation end products on human granulosa cells: implications for women with PCOS

Z. Merhi[a], A. Fadiel[a], E. Buyuk[b], F. Naftolin[a], M. Cipolla[c]

O-276 Wednesday, October 21, 2015 12:30 PM

PlumX Metrics

DOI: https://doi.org/10.1016/j.fertnstert.2015.07.325

Thank you for your attention!

H·E·A·T

H.E.A.T. International Congress on Anti-Aging Medicine
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