Natural Products for Management Highly Infectious Diseases & Metabolic Syndrome

Maurice M. Iwu, Ph.D.

BIORESOURCES DEVELOPMENT GROUP

Viruses

- Viruses are ultramicroscopic, acellular, metabolically inert, nucleoprotein particles containing bundles of gene strands of either RNA or DNA, with or without surrounded by a lipid-containing envelope.
- Unlike free-living bacteria, viruses are obligate intracellular parasites, utilise the host cell machinery to propagate new viruses and can cause ailments as benign as a common wart, as irritating as a cold, or as deadly as the haemorrhagic fever viruses, Ebola, Lassa and Marburg viruses.
- ‘acellular parasites of cellular hosts’

Safe Management and Control of Highly Infectious Diseases

- Early recognition,
- Prompt isolation of the patient(s), and
- Rapid alert of public health authorities.
- Training of healthcare professionals, the group most likely to be initially exposed to an HID and thus responsible for its recognition, should benefit from training that is both targeted and standardized.

Background

- Worst Ebola Outbreak in History – Epidemic in Parts of West Africa
- No Known Cure - No Approved Vaccine or Drug
- Different Hypothesis to Explain the Spread and Virulence

“…drugs and vaccines ought to only play a small part in an overall control strategy.”

Michael Kurilla, Director of the Office of BioDefense at the US-NIH.

- www.thelancet.com Vol 384 August 23, 2014

*"Given that there is no treatment for Ebola virus disease, the main intervention that will determine if someone lives or dies with this infection is supportive care: The ability to replace fluid and electrolytes if a patient is losing them. The ability to replace platelets if that count is low and a patient is starting to bleed. The ability to replace protein in the blood that may be deficient. **A developed country has the capability because of our infrastructure to provide that level of support is at a much higher level than a hospital dealing with patients in West Africa.***

"In the past people thought they needed agents for treatment, and the agents actually turned out to impair people's ability to survive. The focus should remain on aggressive intensive care and the ability to correct abnormalities metabolically, rather than receiving any magic vaccine or product that may or may not improve survival".

Dr. Bruce Ribner, One of the doctors that treated the American Ebola patients. *Scientific American*. Aug 27, 2014

‘‘We can’t solve problems by using the same kind of thinking we used when we created them’’

Albert Einstein (1879–1955)

BDG

BIORESOURCES DEVELOPMENT GROUP

BIORESOURCES DEVELOPMENT
& CONSERVATION PROGRAMME

BIORESOURCES INSTITUTE OF NIGERIA

I H P

INTERCEDD HEALTH PRODUCTS

interCEDD

InterCEDD Laboratories

BIOTRADE

GLOBAL AGENCY LTD

Bioresources Development Group

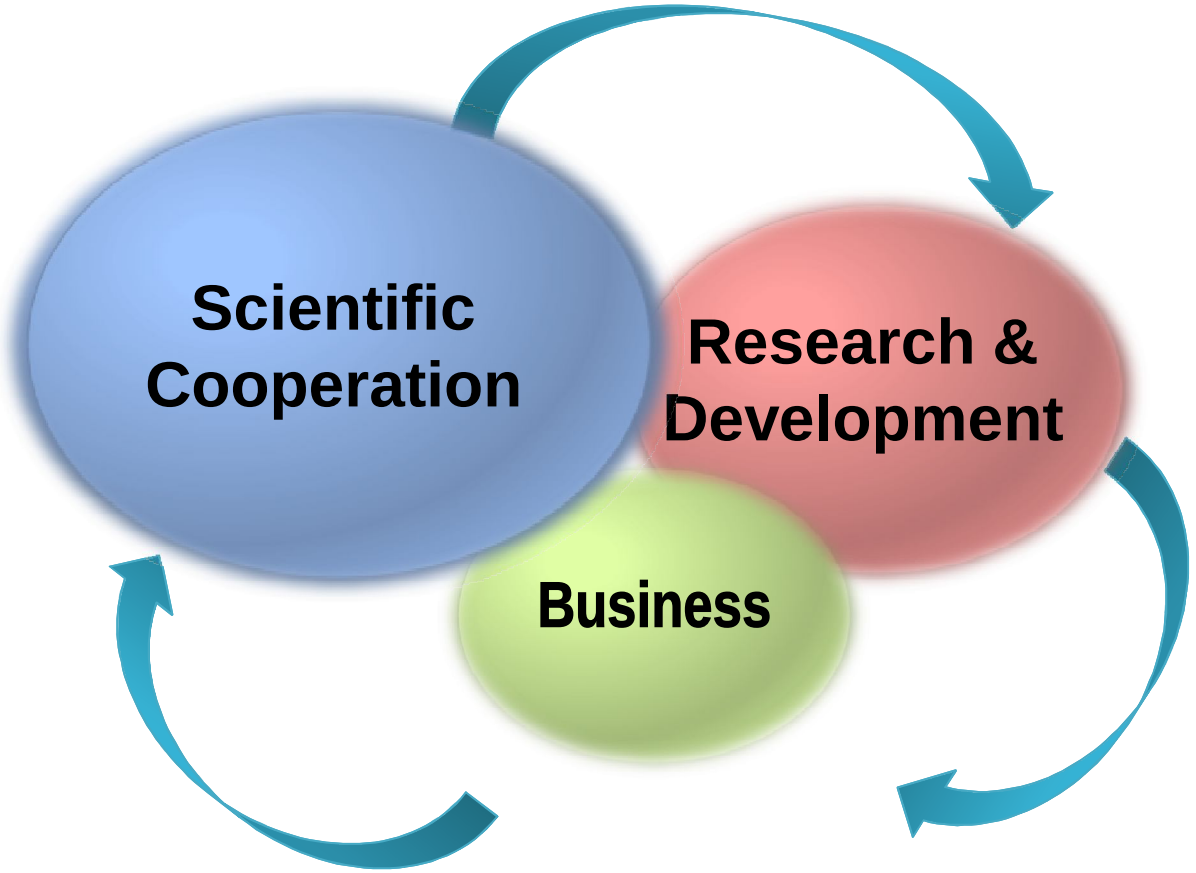
Mission

To promote sustainable utilization of African biological resources for health, economic development and conservation of the biodiversity and develop partnerships with agencies, communities and governments for sustainable development.

Vision

A globally recognized knowledge-creating organization that facilitates the sustainable utilization of natural products for socio-economic development and conservation of the environment.

INTEGRATED TRIPLE-HELIX APPROACH



BDCP - Founded in 1992

- A partnership of academic institutions, scientists, policy experts and industry
- Linking biodiversity, health and economic development of rural areas
- Create a value chain from Farm to Lab to the Market
- Boundary Organization promoting partnerships between industrialized countries and developing countries' institutions in biosciences.

Global Research Capability

- **Bioresources Institute of Nigeria: Coordinates scientific and technical cooperation**

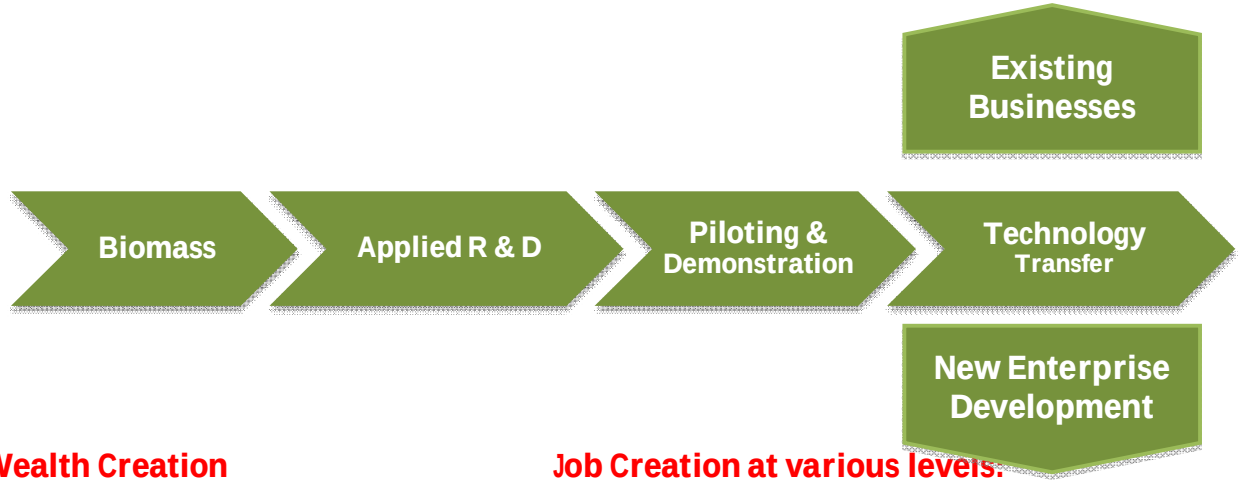
  BDCP operated as a virtual research organization, along with centers of excellence in science and technology as applied to medicinal plant R&D.

  - *USA (Walter Reed Army Institute of Research – WRAIR) - 1994,*
  - *Smithstonian Institution, Pace University, SRI – Alabama - 1998*
  - *Europe - 2002*

Plants + Chem-Biosciences

Industry and practitioners provide input on needs, challenges and opportunities

Bioresources Institute of Nigeria
Networking with FMST, FMA, FMH



Wealth Creation

Poverty alleviation for rural Farmers and farm workers

Increased income for large processors

Export Earning for Nigeria

Job Creation at various levels:

On Farm

Logistics

Processors

Biosciences

Marketing

INDUSTRY

- Industry: Inputs to Primary Production (e.g. seeds, fertilizers, equipment)
- Primary Agricultural and Forestry Production
- Industry: Agricultureal Processing
- Industry: Food, Nutrition and Health Products Manufacturing
- Industry Commodity Wholesale and Storage
- Industry: Industrial Products Manufacturing (e.g. fuels, chemicals, materials.

InterCEDD

InterCEDD

Active in the Following Countries

- Nigeria
- Cameroon
- Kenya
- Guinea
- South Africa
- Senegal
- United States of America

NATURE'S EMPORIUM

Your one stop health shop

- Is a sales center with nation wide outlets in major cities in Nigeria like Lagos, Abuja, Owerri and Enugu with a fitness center.
- We deal on not just IHP products but other natural health products.
- We also promote general wellness by sharing health information to people through our Living well and

  Healthy Magazine, Pamphlets, brochures, Flyers etc.

Bioresources Institute of Nigeria (BION)

Is an institution created under BDG to promote high quality scientific research and training on sustainable utilization of biological resources for health, economic development and conservation of the environment .

- With standard farms at Abuja (Kuje), Benue (Olagbocha) and Imo (Mbano)we grow most of the raw materials we use for manufacturing. BION maintains a world class GMP - processing center at Umuna – Okigwe (Imo State).
- Our yield is chemical free and end products are made from organic ingredients grown without harmful pesticides.
- IHP products are derived from plants grown in BION farms.
- BION conducts training and certification on BION Entrepreneurship and Organic Produce.

IHP Products

S/N	Category	PRODUCT NAME	FEATURES/MAJOR COMPOSITION
1	Teas	Moringa	*Moringa oleifera*
		Bissap	*Hibiscus sabdariffa*
		Ginger	*Zingiber officinalis*
		Hepavital	*Garcinia kola* and *Combretum micranthum*
		Vernonia	Bitter leaf
		Vernonia - Ocimum	*Ocimum gratissimum*, *Curcuma longa*
		Male Tonic	*Garcinia kola*, Aframomum, *Pausinystalia yohimbe*
			Anti-diabetic Kinkeliba Tea
		Esaver	Powdered seeds of Garcinia kola Heckel
		Garcinia	
2	Capsules	Moringa	
		Vernonia	
		Garcinia kola	Adaptogen/ Antioxidant
		Irvingia gabonensis	African Bush Mango
		Erovit and Immunovit	**Based on Asian Mushrooms**
3	Tonics/Bitters	NeutraTonic	Detoxifying Tea/ bitters
4	Herbs	1.Moringa	
		2.Ginger	
		3.Vernonia	
		4. Hibiscus	
5	Infusion	IHP – Bitters	A combination of *Gongronema latifolia*, *Combretum micrantha*, *Andrographis paniculata*, *Garcinia kola*.
6	Liquid/Fluid	Virgin Coconut Oil	Virgin coconut oil
		Honey	Natural Honey
		Cocus nucifera Oil	

EROVIT IHP

ANTI-AGEING SERIES

Rejuvenate Yourself

IHP TEA SERIES

NATURAL TEA FOR HEALTHY YOU

Your Health Drinks

IHP VIRGIN COCONUT OIL

DRUG STORE IN A BOTTLE

For Internal, External Use.
For Cooking.

IHP MORINGA SERIES

FROM THE TREE OF LIFE

Nature's Multivitamins and Minerals

IMMUNOVIT IHP

IMMUNITY SERIES

Manages High Blood Pressure

GARCINIA IHP

BITTER KOLA IN CAPSULES

Boost Your Immunity

Enjoy 100% Quality Organic Dietary Supplements With Zero Additives

I H P
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Owerri: 08062301201, 07017117955

Bioresources Development & Conservation Programme (BDCP)

Nigeria Natural Medicine Development Agency (NNMDA)

International Centre for Ethno - medicine & Drug Development (*InterCEDD*)

Federal Institution of Industrial Research, Oshodi (FIIRO)

The 9th Edition

Present

HERBFEST2016

Symposium

Food as Medicine; African Herbs and Spices as Functional foods and Nutraceuticals.

Call for Abstracts

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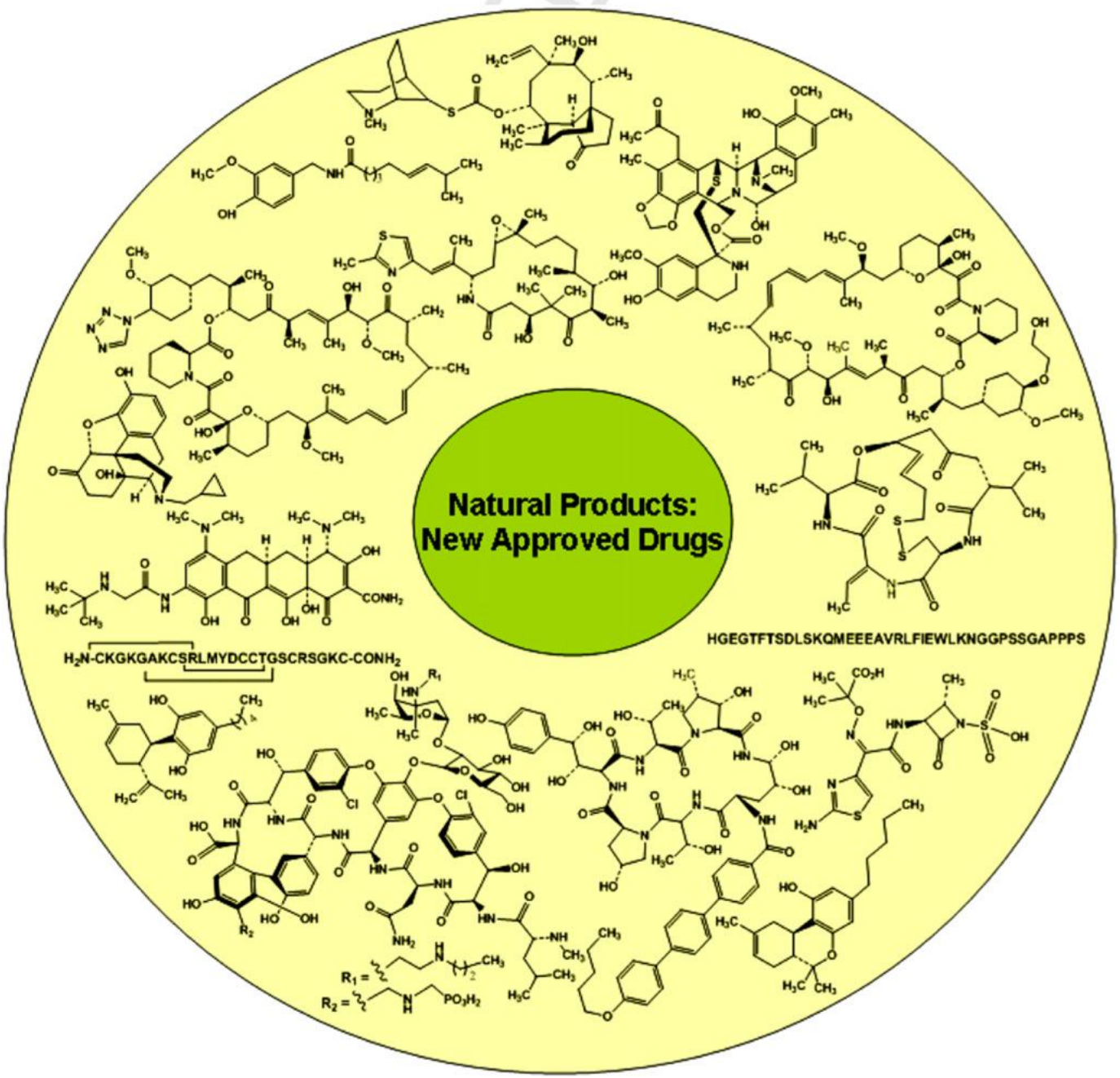
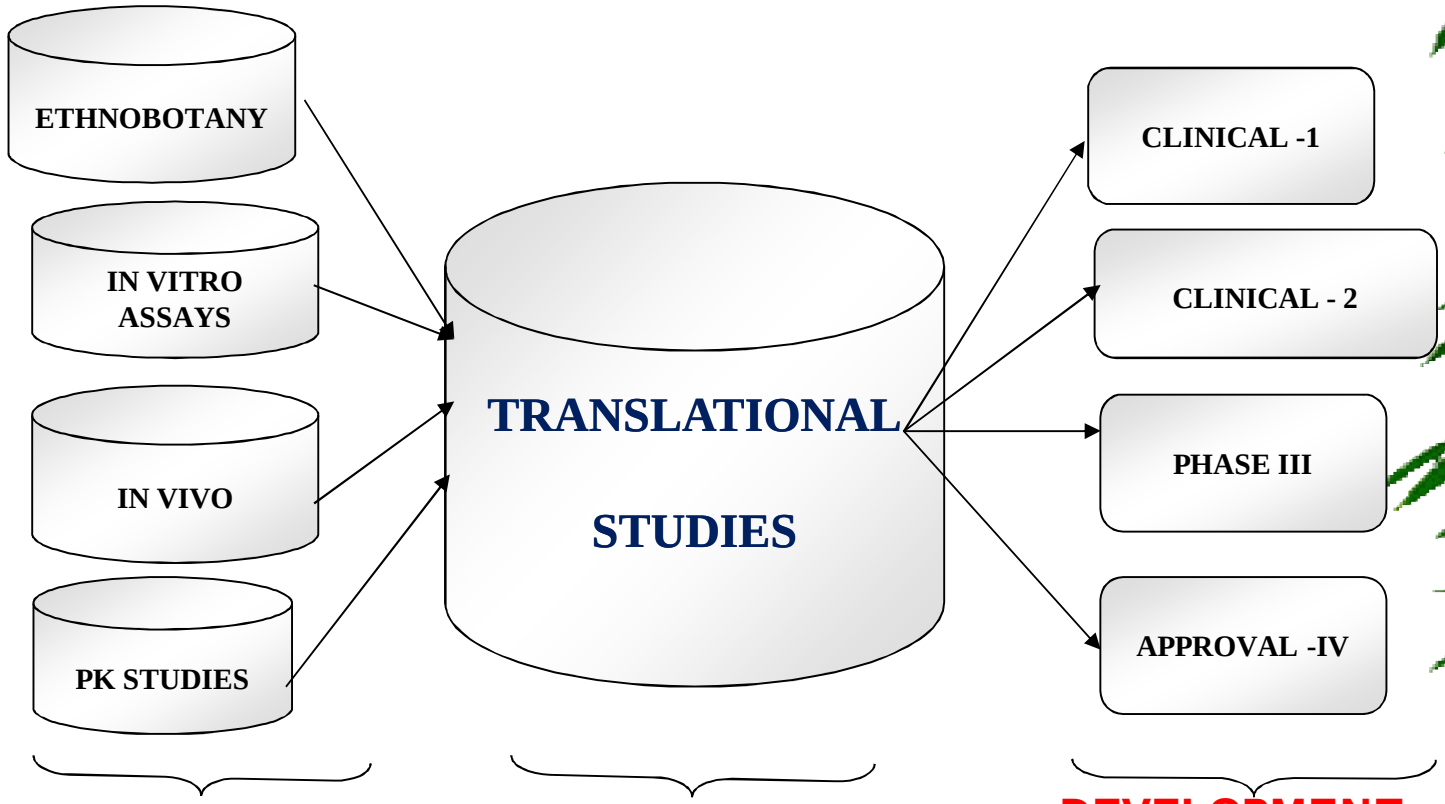
For more information, visit **www.herbfest.com.ng** or email us at **bdcpn@bioresources.org** or call **08160311183, 08092648699**

Natural Products Drugs Approvals 2005 -2010

- A total of 19 NP based drugs were approved for marketing worldwide:
- 7 are classified as NPs,
- 10 as semi-synthetic NPs, and
- 2 as NP derived drugs


Natural Products:
New Approved Drugs
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS
H2N-CKGKGAKCSRLMYDCCTGSCRSGKC-CONH2

DRUG DEVELOPMENT BOXES



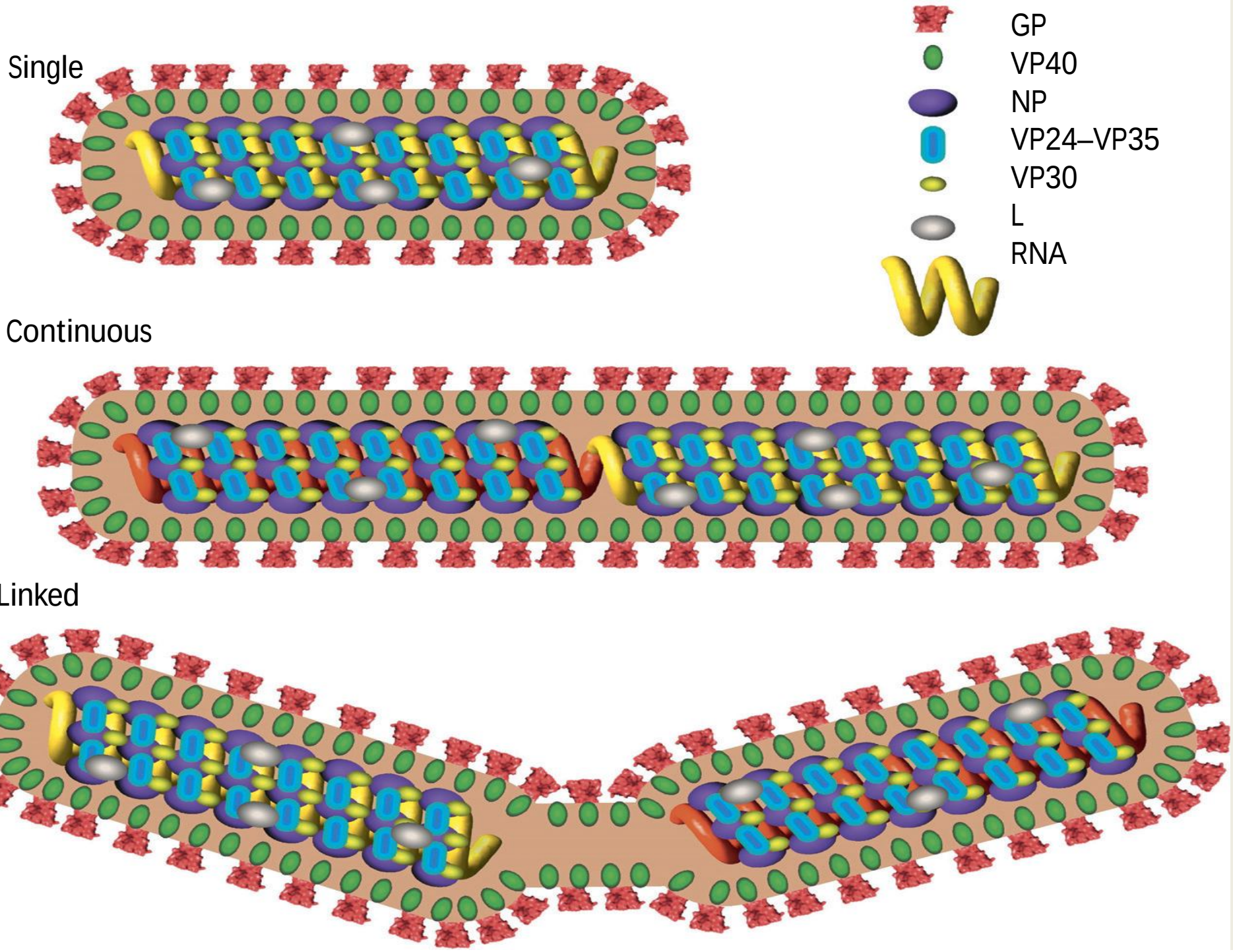
EVD Treatment Strategy

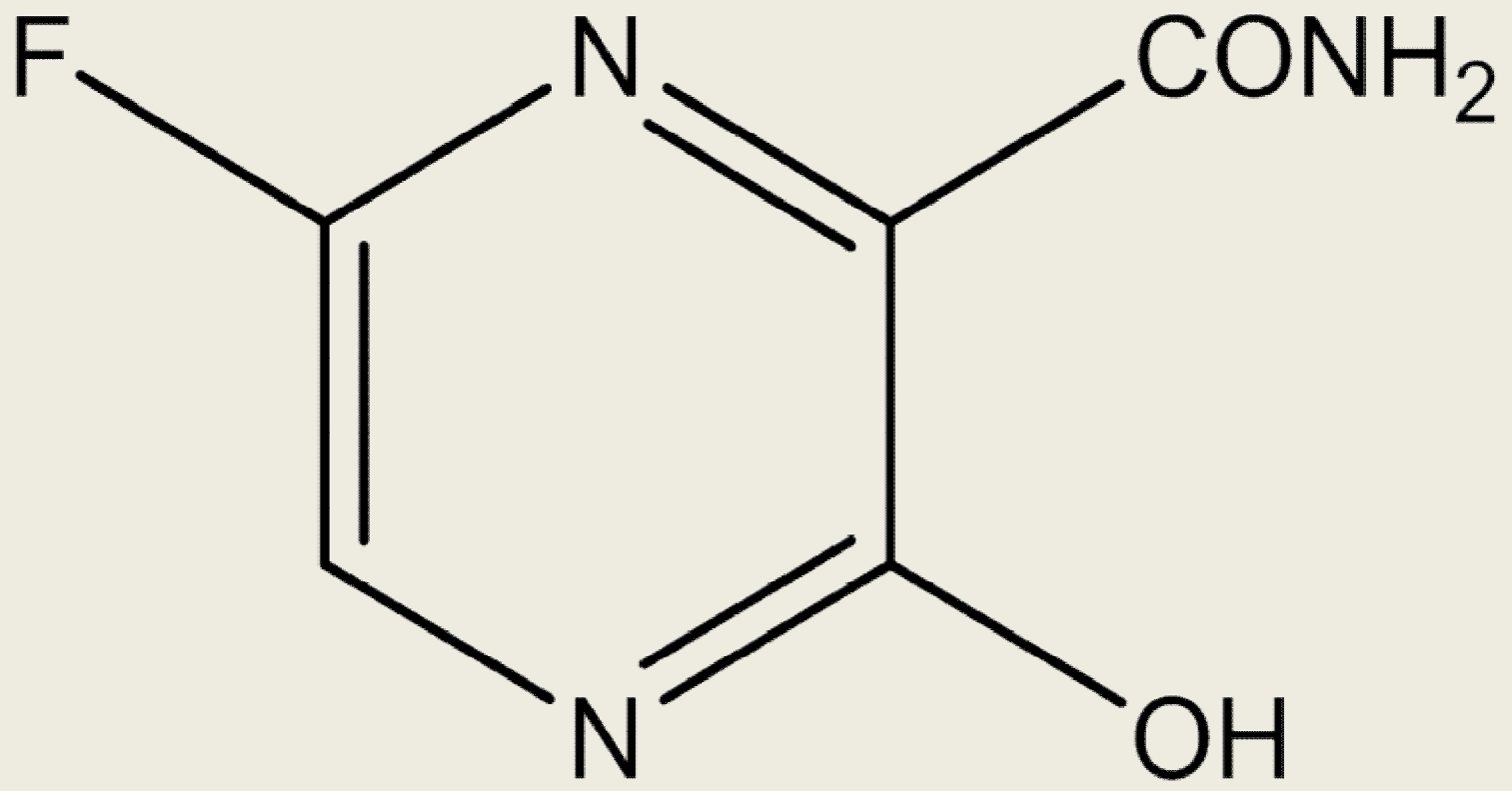
- Antiviral Agents
  - Virus Targeting Antivirals (VTAs)
    - Direct Virus Targeting Antivirals (DVTAs)
    - Indirectly Virus Targeting Antivirals (InDVTAs)
  - Host Targeting Antivirals
    - Interferon (IFN)
    - Cyclophilin Inhibitors
- Immunotherapies
- Pathogenesis Based Interventions/ Support

Experimental Drugs for EVD

- Novel Chemical Entities From Screening Programmes and In Silico Experiments

- Re-Purposed Drugs: These are approved drugs already in clinical use for different indication (s) other than EVD.
- Because of the complications of conducting Phase 3 clinical studies for EVD, Re-Purposing may be the preferred source.


Single
Continuous
Linked
GP
VP40
NP
VP24–VP35
VP30
L
RNA

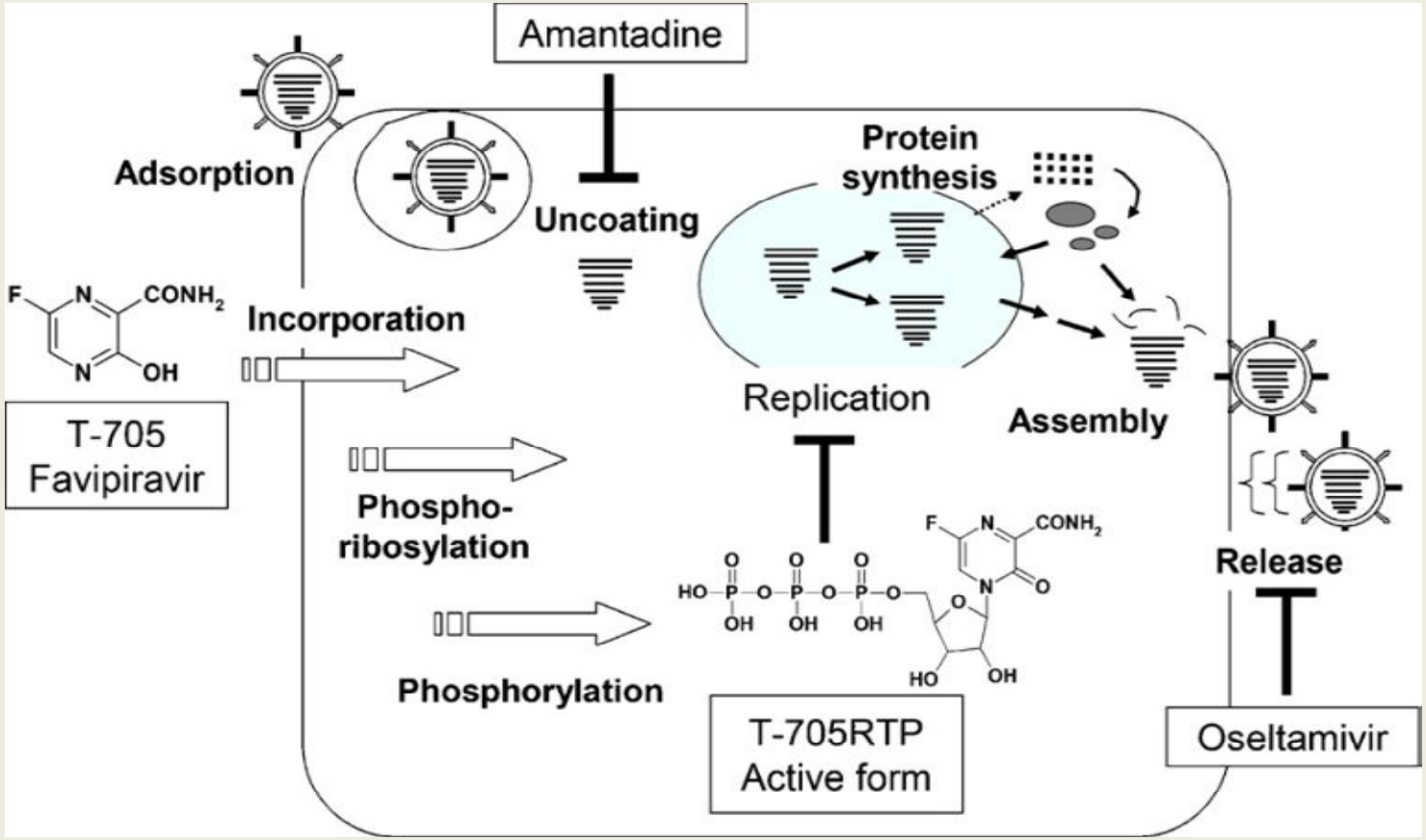


Favipiravir

FAVIPIRAVIR – Oral Antiviral

- Favipiravir (6-fluoro-3-hydroxy-2-pyrazinecarboxamide), originally known as T-705, and the related compounds were discovered and synthesized by Toyama Chemical Co., Ltd. Toyama. Japan. The proprietary licensed products are also being promoted by U.S. firm MediVector and the Canadian company, Tekmira.

- Exhibited *in vitro* and *in vivo* activity against *Ebola virus.*
- Phase III clinical evaluation of Favipiravir for influenza therapy has been completed in Japan. Phase 3 on going in U.S.A.



Mode of action of Favipiravir and other anti-influenza drugs. Favipiravir is converted to the ribofuranosyl triphosphate form and inhibits influenza virus RNA polymerase in the host cells host cells. Amantadine inhibits virus M2 proteins, and oseltamivir inhibits the release of virus.
– After Y. Furuta et al. *Antiviral Research* **82** (2009) 95–102**.**

Antiretroviral Drugs

Drugs used to treat HIV infection have been found active against Ebola virus and may be useful in EVD.

Azidothymidine

Lamivudine

Zidovudine

Nevirapine

Tenofovir

Tipranavir

SCYTOVIRIN (SVN)

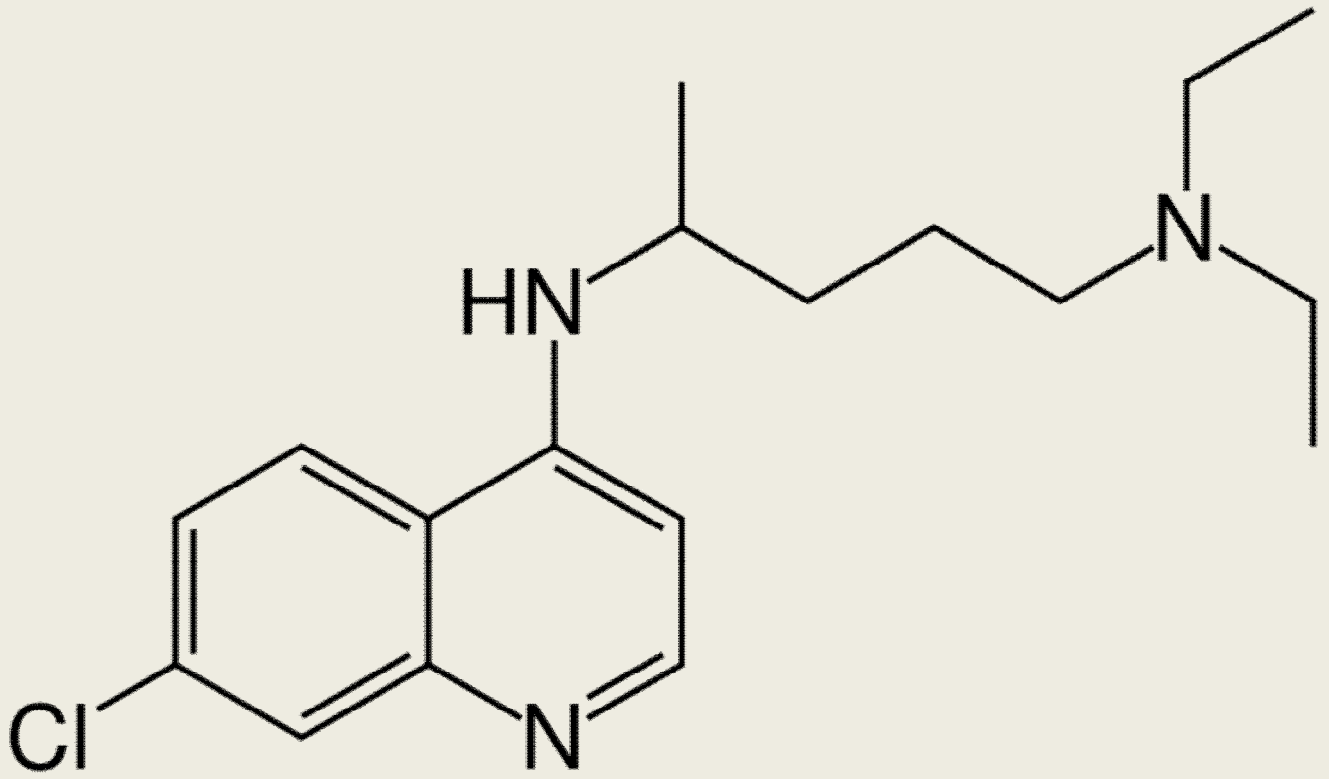
(cyanobacterial lectin – from *E. coli*.

In Vitro* and *In Vivo* activity against *Ebola virus.

- 30 mg/kg/day of SVN by subcutaneous injection every 6 h, beginning the day before virus challenge, 9 of 10 animals survived the infection
- When given one hour or one day after challenge, 70–90% of mice survived

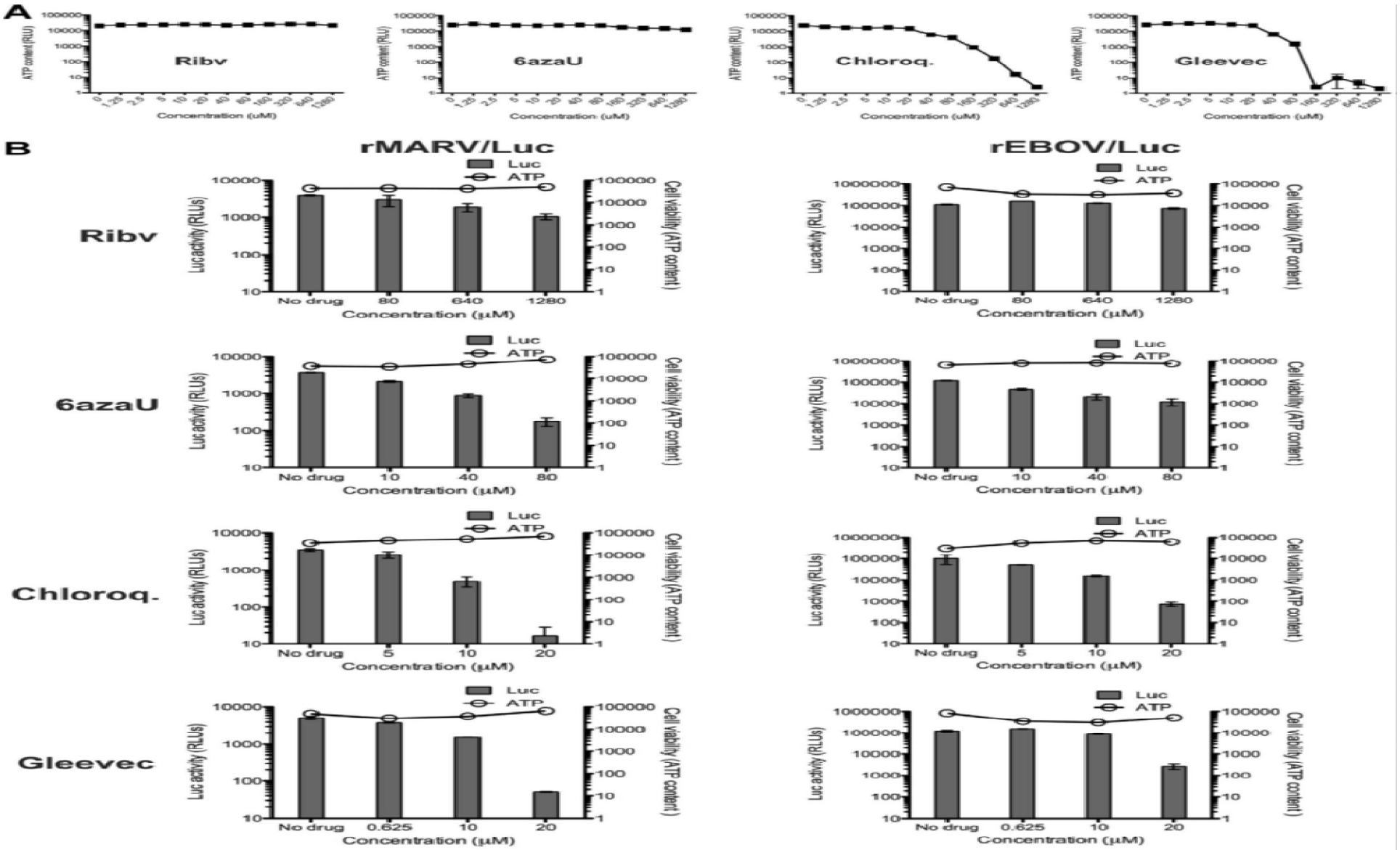
Active against Angola strain of the related *Marburg virus*. - Garrison, A.R et al (2014) *Antiviral Research* (in press).

CHLOROQUINE



CHLOROQUINE ANTIVIRAL ACTIVITY

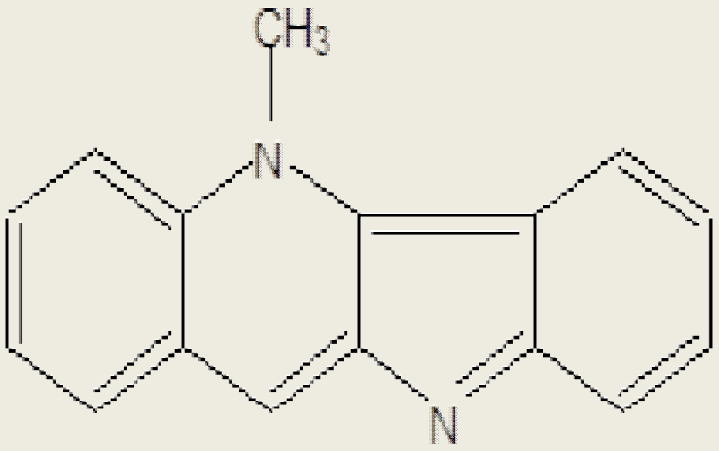
- Direct antiviral effects, inhibiting pH-dependent steps of the replication of several viruses including members of the flaviviruses, retroviruses, and coronaviruses.
- Active against HIV replication, in clinical trials.
- Immunomodulatory effects, suppressing the production/release of tumour necrosis factor and interleukin 6, which mediate the inflammatory complications of several viral diseases, and may include Ebola virus.



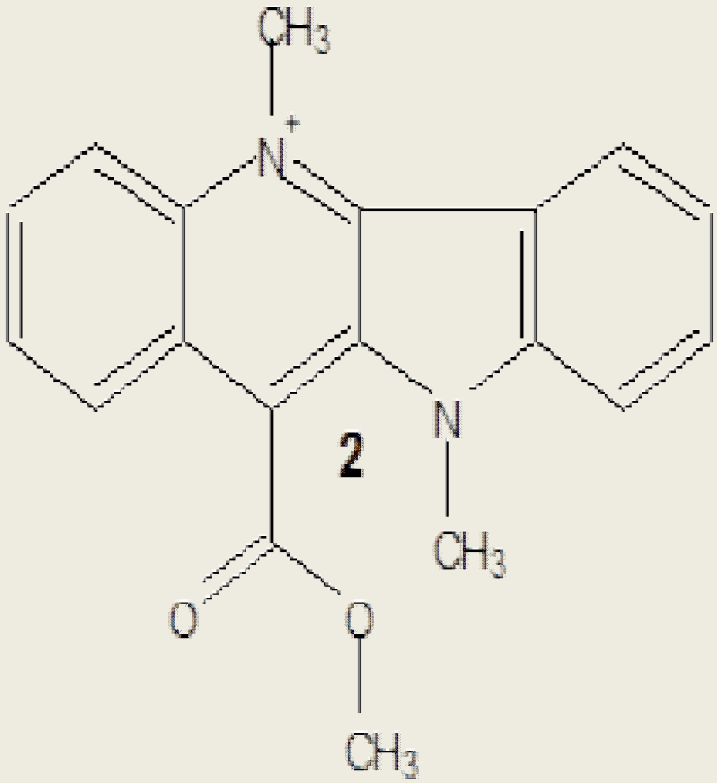
C

	Ribavirin (80 1280 μM)	6azaU (80 μM)	Chloroq. (20 μM)	Gleevec (20 μM)
rMARV/Luc	26 73	95	99.5	99
rEBOV/Luc	0 35	90	99.3	98

Reduction of Luc signal (%)

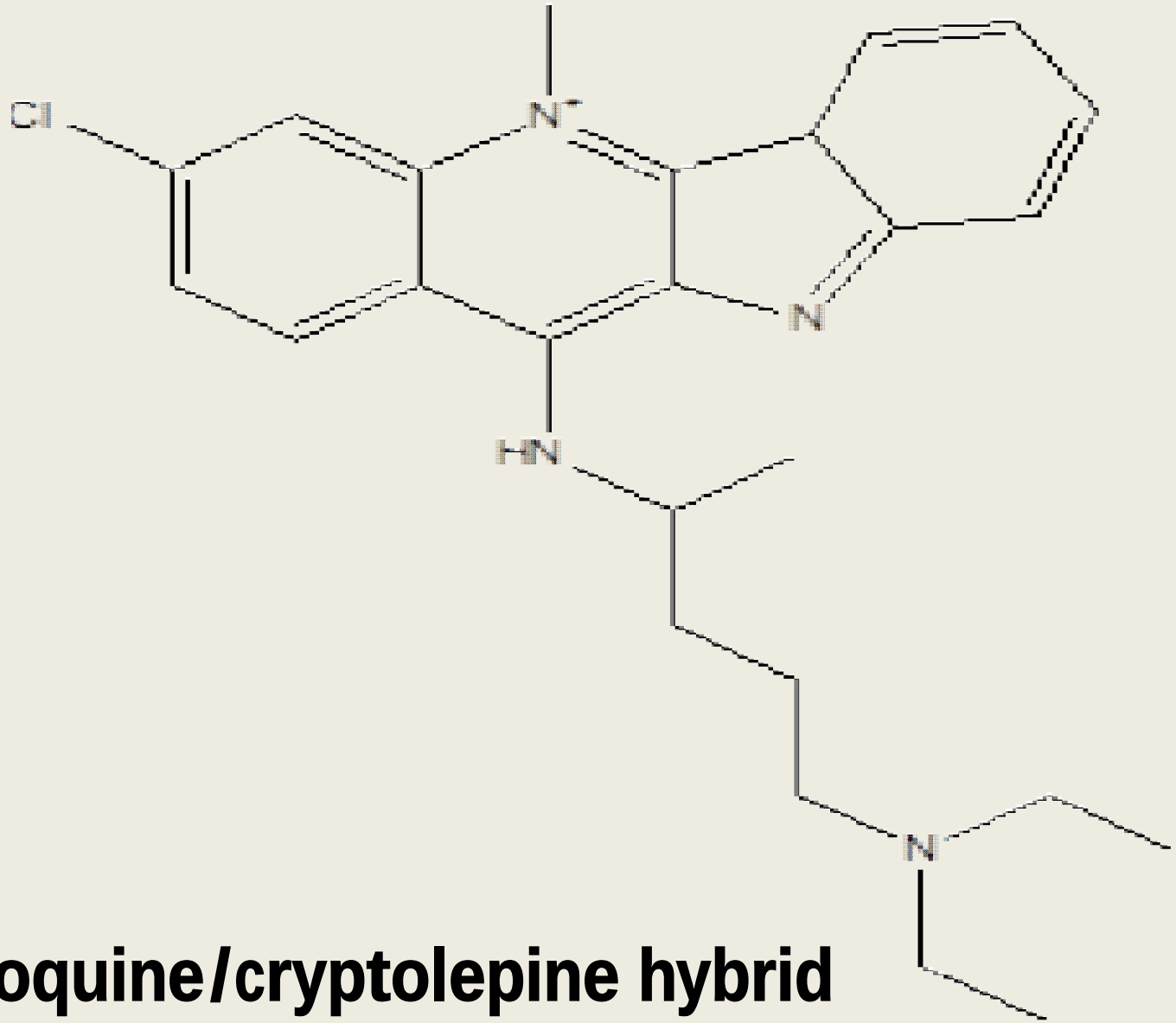


1



2

Cryptolepine (**1**) and one of its analogues, Sanguinolentine (SP910165) (**2**).



Chloroquine/cryptolepine hybrid
(SU2953)

CNN interactive CNN.com

Africa-born scientist says plant may be Ebola cure

August 3, 1999
Web posted at: 5:28 PM EDT (2128 GMT)

ST. LOUIS (Reuters) -- Compounds found in a plant used by West African faith healers stopped the spread of the deadly Ebola virus in lab tests and may be effective against the flu, a scientist told a botany conference on Tuesday.

The Garcinia kola plant, whose seeds are often included in welcoming food baskets in Africa where it grows wild, contains compounds with two flavonoid molecules fused together that scientists believe halted the spread of Ebola in tests.

"This is a very exciting discovery. The same forest that yields the dreaded Ebola virus could be a source of the cure," Maurice Iwu, founder of the London-based Bioresources Development and Conservation Program, told the International Botanical Congress.

Flavonoids, which can be found in tea and in wine, are known to neutralize harmful chemicals that damage cells and can lead to illnesses such as heart attacks, strokes and cancer.

Iwu, who was born to a family of healers in Nigeria and trained in pharmacology, was led to the plant by traditional healers who said it had been eaten for thousands of years. Iwu said the compounds were nontoxic in animal tests.

The plant's flavonoid compounds that were believed to offer the healing powers could form the basis for drugs in a few years, he said. Tests on some compounds from the plant were also effective against some strains

HEALTH LATEST

Thursday, August 5, 1999 Published at 14:34 GMT 15:34 UK

Health

Ebola cure hope

Four out of five people who get infected die

A plant has been found to halt the deadly Ebola virus in its tracks in laboratory tests, scientists have said.

The extract can be eaten or rubbed into the skin

They used a compound from Garcinia kola, a plant commonly eaten in West Africa. Compounds from the plant have also proved effective against some strains of flu.

If the anti-Ebola compound proves successful in animal and human trials, it will be the first medicine to successfully treat the virus that causes Ebola haemorrhagic fever - an often-fatal condition.

The discovery was announced at the 16th International Botanical Congress in St Louis in the US.

Four deaths per five cases

The Ebola virus was first documented in 1976 after an outbreak in Zaire - now the Democratic Republic of the Congo - where 88% of the 318 human cases died.

Garcinia kola Seeds

Respiratory tract infections

Anti-inflammatory

Antiviral

Tonic

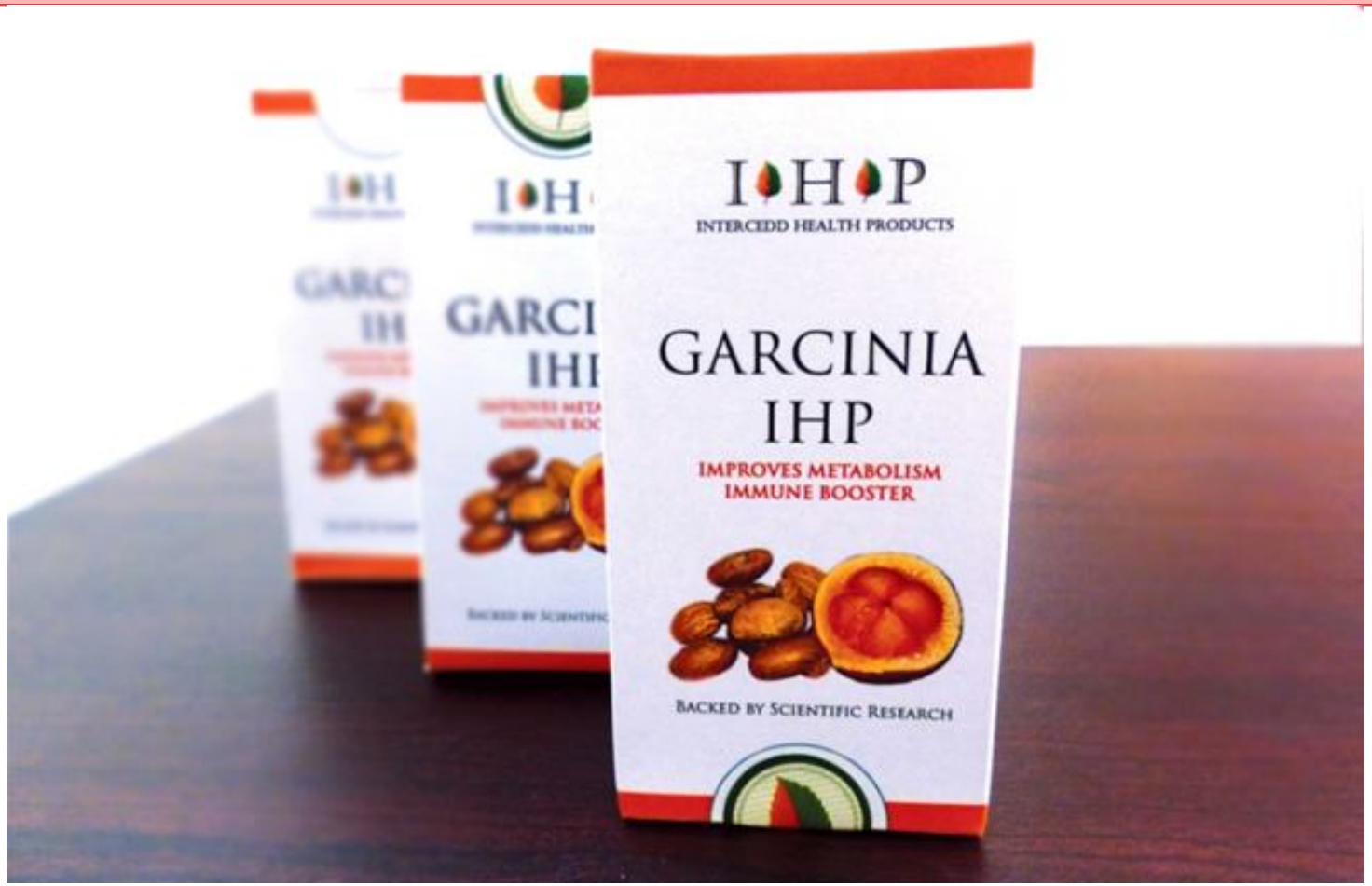
Garcinia kola: Potential Medicinal Agents

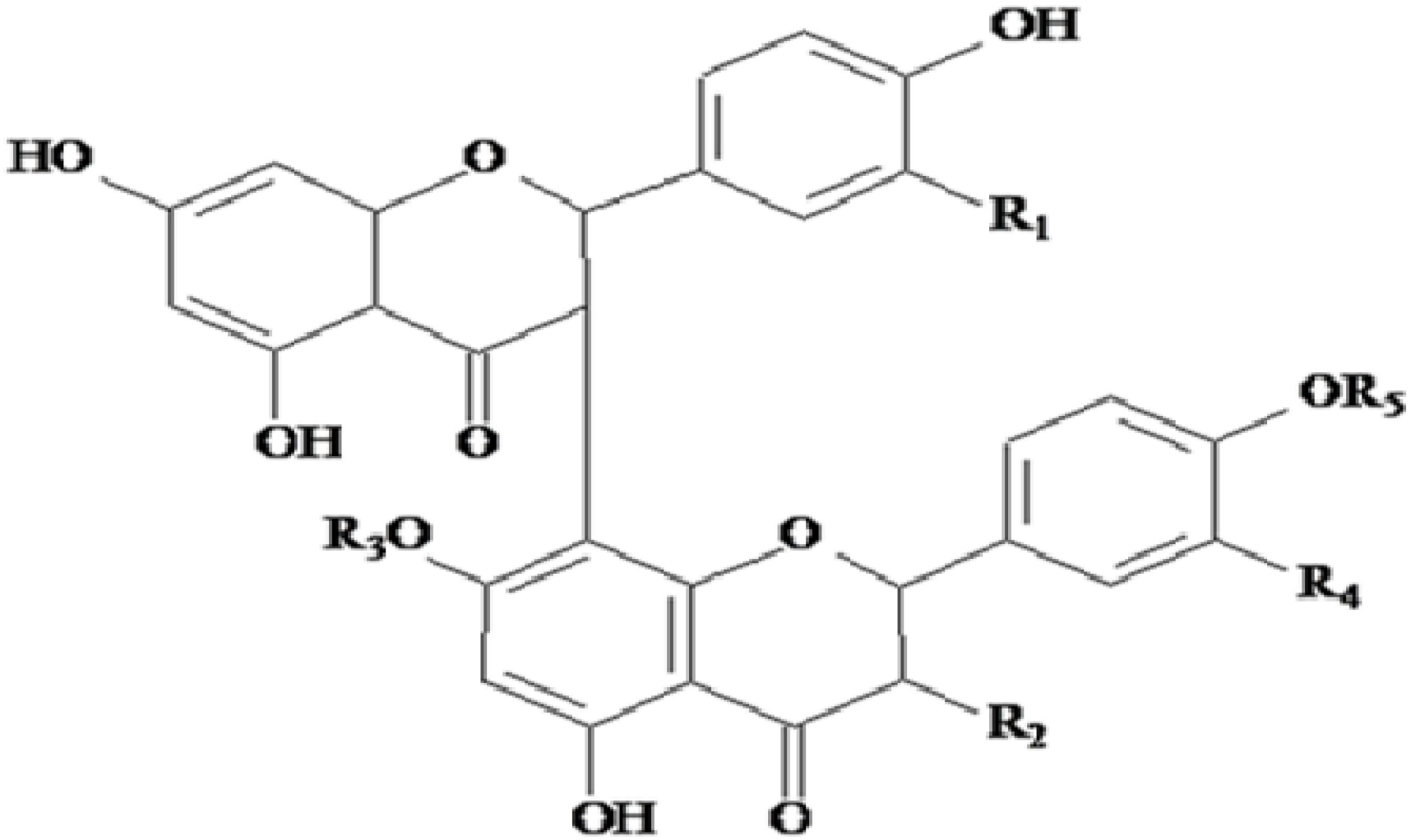
- Whole Seeds: Standardized (CCC and HPTLC) With Respect to the Biflavonoid Content – Dietary Supplement;
- Total Extract (60% Ethanol): Standardized Using GB-1 and Garcinol as the markers: Dietary Supplement;
- Kolaviron – Biflavonoids of *G. kola*, standardized by HPTLC to conform to 2:2:1:1, Kolaflavanone, GB-1, GB-2 and GB-1 glycoside respectively: Phytomedicine;
- GB-1 and its glycoside – Active Chemical Entity: Drug
- Hydroxy Cinnamic Acid – Isolated from the Rind:

Garcinia kola - Pharmacology

- Anti-inflammatory
- Anti-microbial
- Anti-viral
- Anti-oxidant
- Immunomodulator
- Anti-hepatotoxic

Garcinia-IHP





		R1	R2	R3	R4	R5
1	GB-1a-glucoside	H	H	glc	H	H
2	GB-1[a]	H	H	H	H	H
3	GB-1	H	OH	H	H	H
4	GB-2	H	OH	H	OH	H
5	Kolaflavonone	H	OH	H	H	CH3

Kolaviron

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Year | Source title | Author name | Affiliation name | Country | Document type | Subject area

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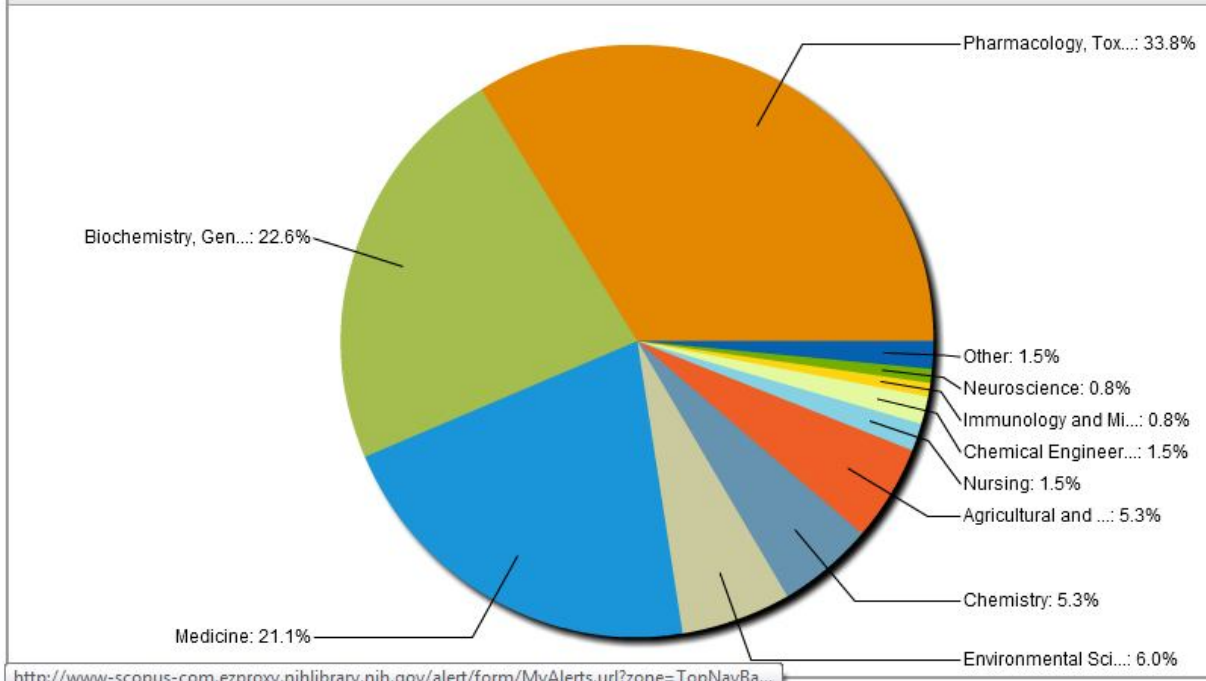
Subject Areas This chart shows the total number of documents for this query by Subject Area.



Subject Area	Documents
Pharmacology, Toxicology and Pharmaceutics	45
Biochemistry, Genetics and Molecular Biology	30
Medicine	28
Environmental Science	8
Chemistry	7
Agricultural and Biological Sciences	7
Nursing	2
Chemical Engineering	2
Undefined	1
Neuroscience	1
Immunology and Microbiology	1
Health Professions	1
Total	133

http://www-scopus-com.ezproxy.nihlibrary.nih.gov/alert/form/MyAlerts.url?zone=TopNavBa...

Kolaviron

- Hepatoprotective properties have been demonstrated in 68 published studies.
- Kolaviron protects against carcinogen-induced hepatotoxicity by free radical scavenging, metal chelation, upregulation of the detoxification system, inhibition of stress response proteins, and downregulation of NF-kB and AP-1.
    - Farombi, E.O. (2011) In: V.R. Preed, R.R. Watson, and V.B. Patel (Eds.), *Nuts and Seeds in Health and Disease Prevention. New York: Elsevier, Chapter 26, p. 221).*

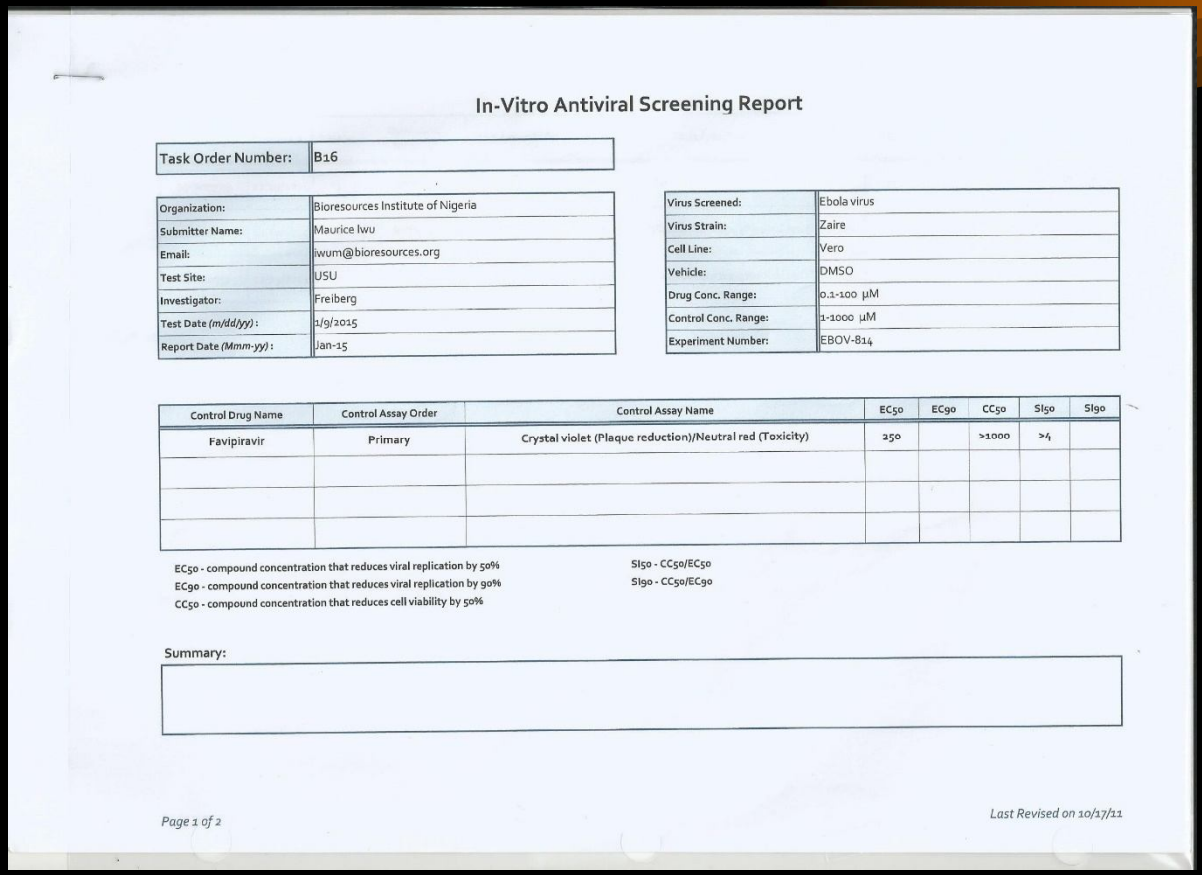
Antiviral Activity of Kolaviron

- The biflavonoids of the seeds of *Garcinia Kola* Heckel have shown remarkable broad spectrum antiviral activity *in vitro* against a variety of viruses including Punta Toro, Pichinde, Sandfly fever, Influenza A, Venezuelan Equine Encephalomyelitis and Ebola, with IC_{50} values of 7.2-32 µg/ml and MTC of more than 320 µg/ml. (Iwu, M.M. *et al*., 2002. In: Iwu and Wootton (Eds.), *Ethnomedicine and Drug Discovery*. Amsterdam: Elsevier Science, Chapter 17, p. 191.

NIAID –BION Non-Clinical Evaluation Agreement

- Cooperative Research Agreement Between Bioresources Institute of Nigeria and the U.S. National Institute of Allergy and Infectious Diseases – September 5th 2014.
- Evaluation of Compounds Submitted by BION for Activity Against Ebola.
- Covers Pre-Clinical and Non-Clinical Tests

Retesting of Kolaviron Jan 2015



In-Vitro Antiviral Screening Report

Task Order Number:	B16

Organization:	Bioresources Institute of Nigeria
Submitter Name:	Maurice Iwu
Email:	iwum@bioresources.org
Test Site:	USU
Investigator:	Freiberg
Test Date *(m/dd/yy)* :	1/9/2015
Report Date *(Mmm-yy)* :	Jan-15

Virus Screened:	Ebola virus
Virus Strain:	Zaire
Cell Line:	Vero
Vehicle:	DMSO
Drug Conc. Range:	0.1-100 µM
Control Conc. Range:	1-1000 µM
Experiment Number:	EBOV-814

Control Drug Name	Control Assay Order	Control Assay Name	EC50	EC90	CC50	SI50	SI90
Favipiravir	Primary	Crystal violet (Plaque reduction)/Neutral red (Toxicity)	250		>1000	>4	

EC50 - compound concentration that reduces viral replication by 50%
EC90 - compound concentration that reduces viral replication by 90%
CC50 - compound concentration that reduces cell viability by 50%

SI50 - CC50/EC50
SI90 - CC50/EC90

Summary:

Page 1 of 2

Last Revised on 10/17/11

Retesting of Kolaviron Jan 2015

Screening Results

ARB No.	Date Received m/dd/yy	Trial No	Compound Name/ID	Drug Assay Order	Drug Assay Name	EC50	EC90	CC50	SI50	SI90
14-000929	12/19/2014	1	BION-14	Primary	Crystal violet (Plaque reduction)/Neutral red (Toxicity)	25		>100	>4	
14-000930	12/19/2014	1	BION-15	Primary	Crystal violet (Plaque reduction)/Neutral red (Toxicity)	25		>100	>4	
14-000931	12/19/2014	1	BION-16	Primary	Crystal violet (Plaque reduction)/Neutral red (Toxicity)	10		13.3	1.3	

Anti-Ebola in vitro Assay 2015

- The antiviral *in vitro* Assay against Ebola virus (Zaire) was conducted under agreement with the United States National Institute of Health (US-NIH) Antiviral Screening Program at Utah State University. Institute for Antiviral Research. Vet Science/Bacteriology Bldg Room 204. 5600 Old Main Hill Logan, UT 84322-5600. U.S.A. Using a Vero cell line, with the compound (ARB 14-000929) was dissolved in DMSO and tested at concentrations of 0.1 – 100 μM; the control Favipiravir was tested at concentrations of 1 – 1000 μM.

Anti-Ebola Activity of 'Akiiluvir' from Garcinia kola Jan-2015

	Favipiravir	**Akiiluvir**
• EC_{50} –	250 μM	25 μM
• CC_{50} –	>1000	>100 μM
• SI_{50} – CC_{50}/ EC_{50}	> 4	>4

Kolaviron

- Kolaviron has been shown to interfere with LPS signalling by reducing the activation of several inflammatory transcription factors and that its inhibitory action on IL-6 secretion correlates with inhibition of ERK1/2, p38, Akt, p-c-JUN and JNK signalling pathways - Abarikwu, S.O. (2014). *Biochimica et Biophysica Acta* **1840**: 2373–2381

KOLAVIRON - 2

- Inhibition of dimethyl nitrosamine-induced hepatotoxicity by suppressing COX-2 and iNOS expression: NF-kB and AP-1 as potential molecular targets. - Farombi, E. O *et al*. 2009.*Life Sciences*, 84: 149 -155.

- protective effects on the neurons of the hippocampus and cerebellum of malnourished mice challenged with the neurotoxin, 3-Nitropropionic acid; inhibition of tyrosinase

Ajayi, S.A. *et al.*, 2011. *Asian Pacific Journal of Tropical Biomedicine* . 261-265); Okunji, C.O. et al. 2007. *J. Chromatography* A. **1151**: 45-50

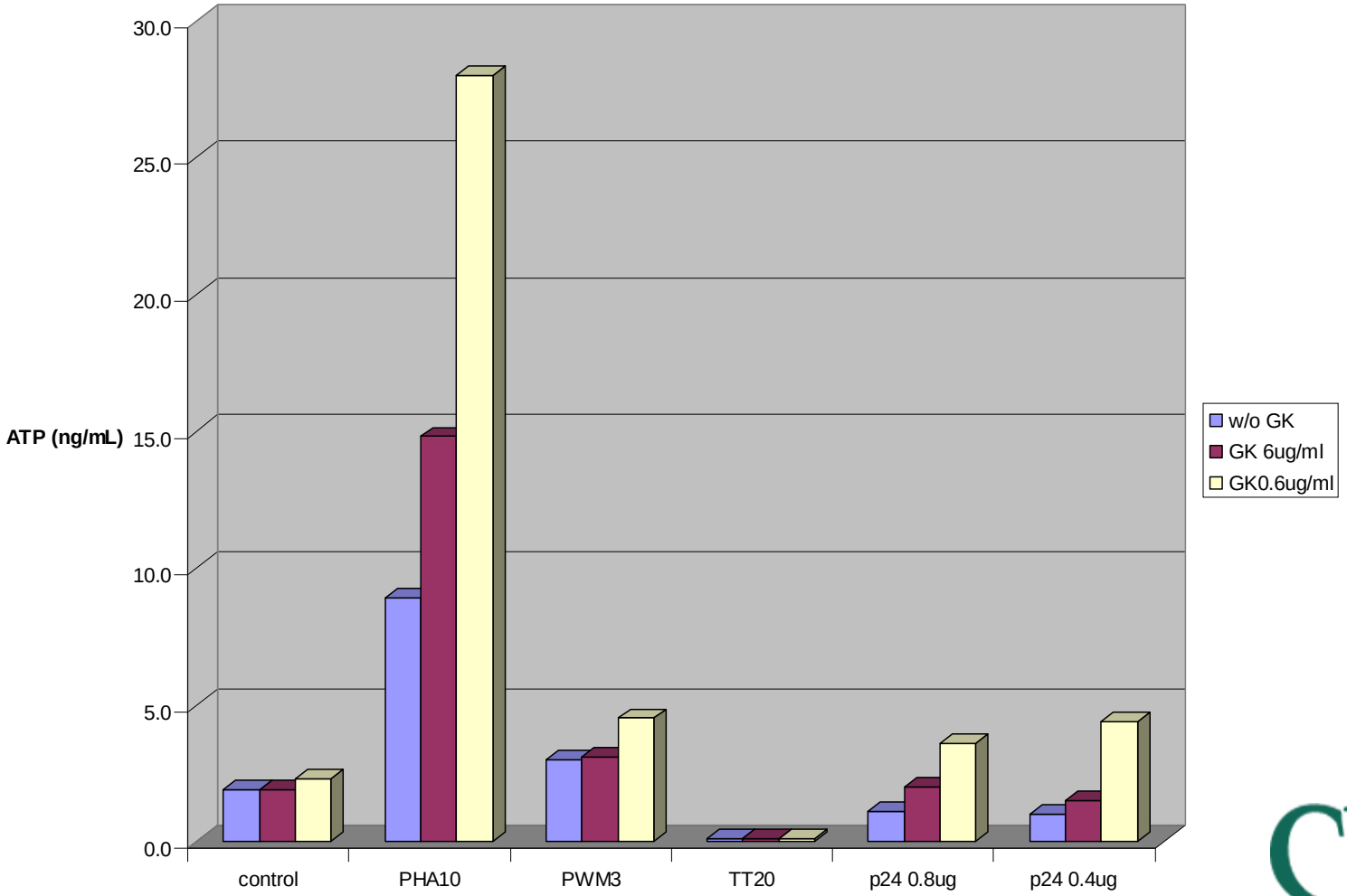
Kolaviron - 3

- It is proposed that because *Garcinia kola* constituents have both antiviral activity and remarkable inhibitory activity against pro-inflammatory cytokines and chemokines, with a long history of safety, that Garcinia biflavonoids should be evaluated for possible use in the early management of human exposure to Ebola virus and/or treatment of the disease, as a means of controlling the massive viral replication and also ameliorate the dysregulated inflammation associated with the onset of the infection.

Immunopotentiating properties of Garcinia kola *in vitro*

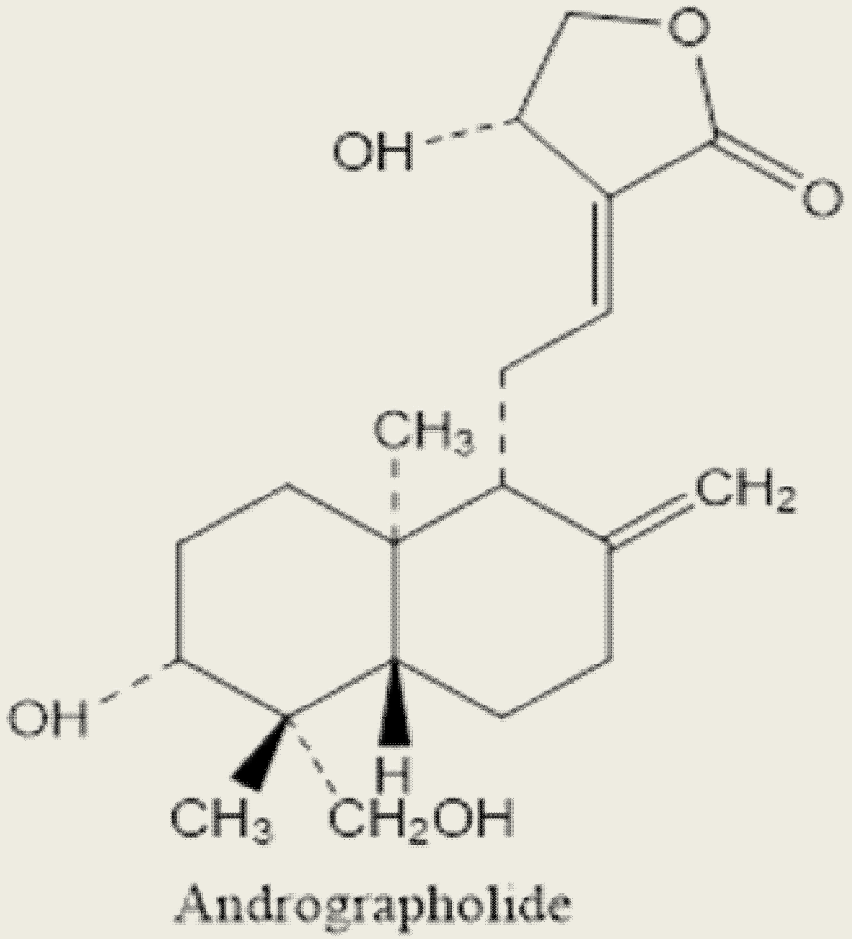
BDCP and CYLEX incorporated Collaboration

Garcinia kola enhanced ATP response in lymphocytes from HIV infected patient



CYLEX incorporated

Experimental Antiviral Agents from Nigerian Plants

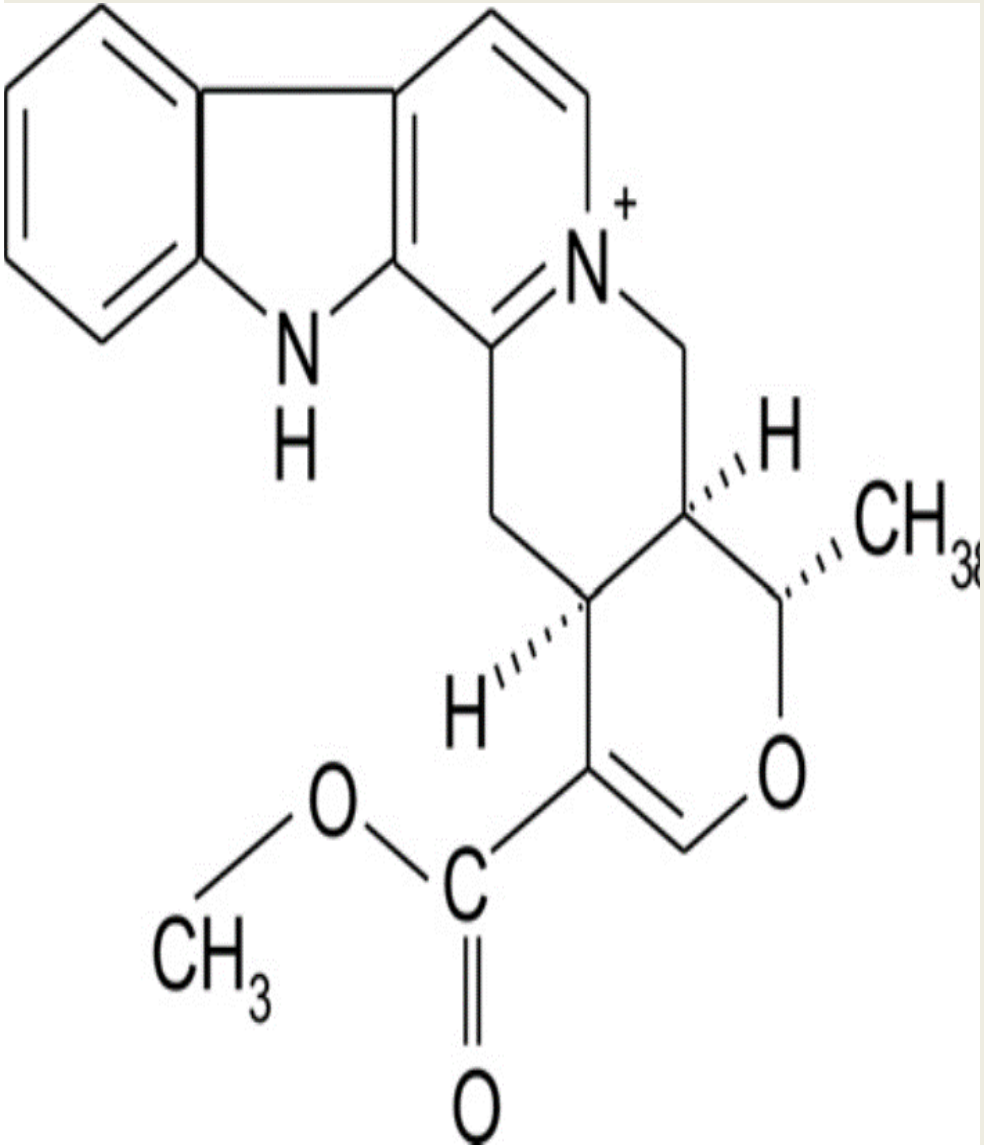


Andrographolide

Active Against

- HIV
- Ebola
- SARS
- MERS

Experimental Antiviral Agents from Nigerian Plants



- Original activity for:
  - Prostrate Cancer (Bemis *et al*: INTERNATIONAL JOURNAL OF ONCOLOGY 29: 1065-1073, 2006)
  - Antipsychotic, schizophrenia (Iwu *et al*: Pharmacology, Biochemistry and Behavior 77 (2004) 481–489; Linck *et al*: Progress in Neuro-Psychopharmacology & Biological Psychiatry 36 (2012) 29–33).
- In Vitro Activity Against Ebola virus by BION/NIH Study

Metabolic Syndrome

- World-wide increase in the rate of the incidence of obesity, type 2 diabetes mellitus (T2DM), hypertension, and metabolic syndrome (MetS).

- **Several studies have implicated increased consumption of calorie-rich/high-fat diet, lack of exercise, and sedentary lifestyles as some of the likely causes. But some scientists argue that increased consumption of a carbohydrate-rich diet with enhanced contents of sucrose, fructose, or glucose, orcombination of all three in ready-to-eat foods is responsible for the increasing incidence of obesity, T2DM, and MetS.**

Two Factors Targeted in Our Intervention

- Sugars – Especially Fructose in the form of High Fructose Corn Syrup (HFCS)
- Oxidative Stress and Pro-inflammatory agents

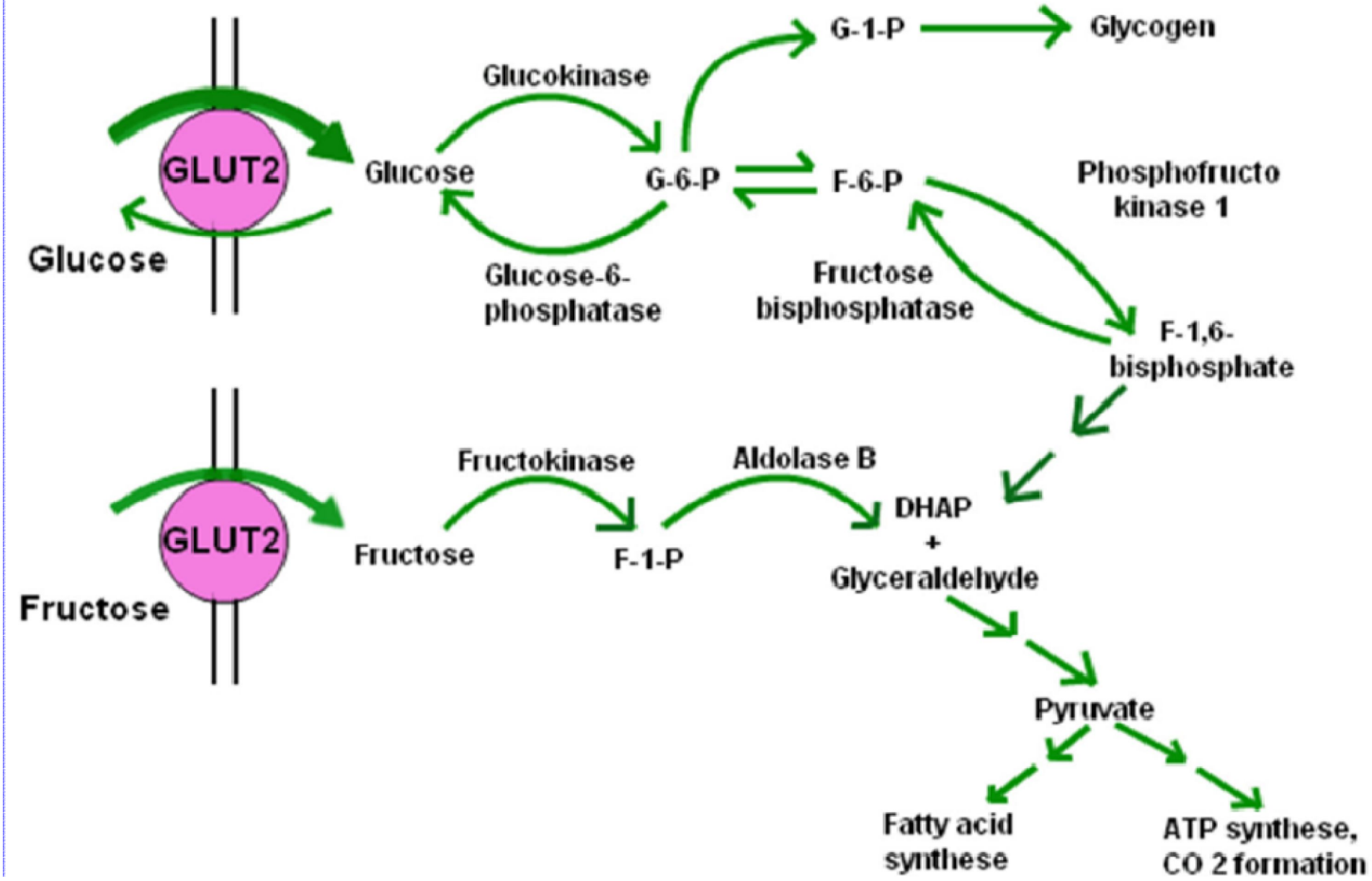
Sucrose Vs HFCS

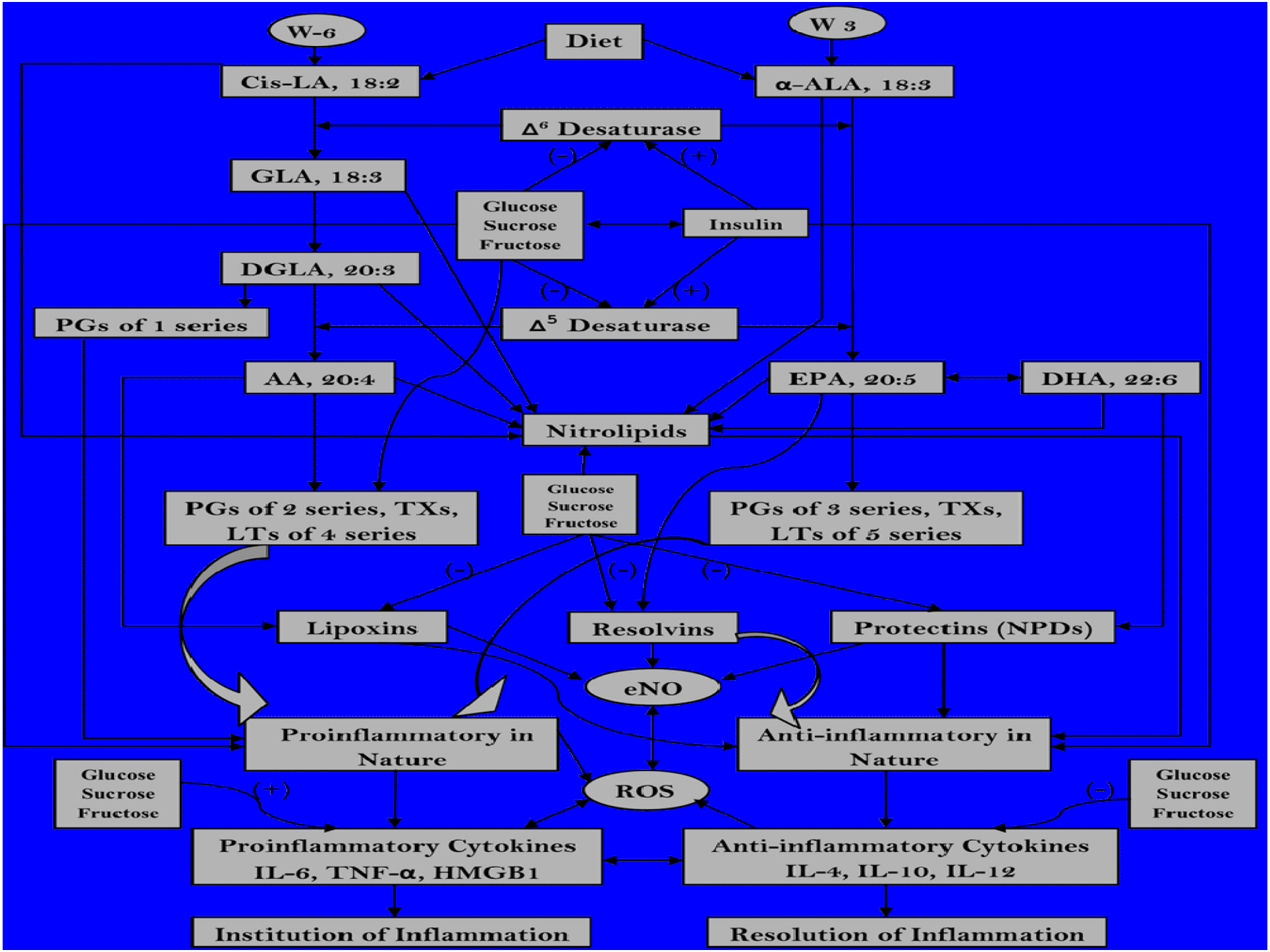
- Sucrose is composed of equal amounts of the two simple sugars (i.e. 50 %t fructose and 50 % glucose) but the typical high-fructose corn syrup (HFCS -55) features an imbalanced ratio, containing 55 percent fructose and 42 percent glucose.
- Larger sugar molecules called higher saccharides (oligomers) make up the remaining 3 percent of the sweetener. Other varieties of HFCS available commercially are HFCS – 42 and HFCS – 90 (the numbers reflect the percentage of fructose they contain).

Sucrose Vs HFCS - 2

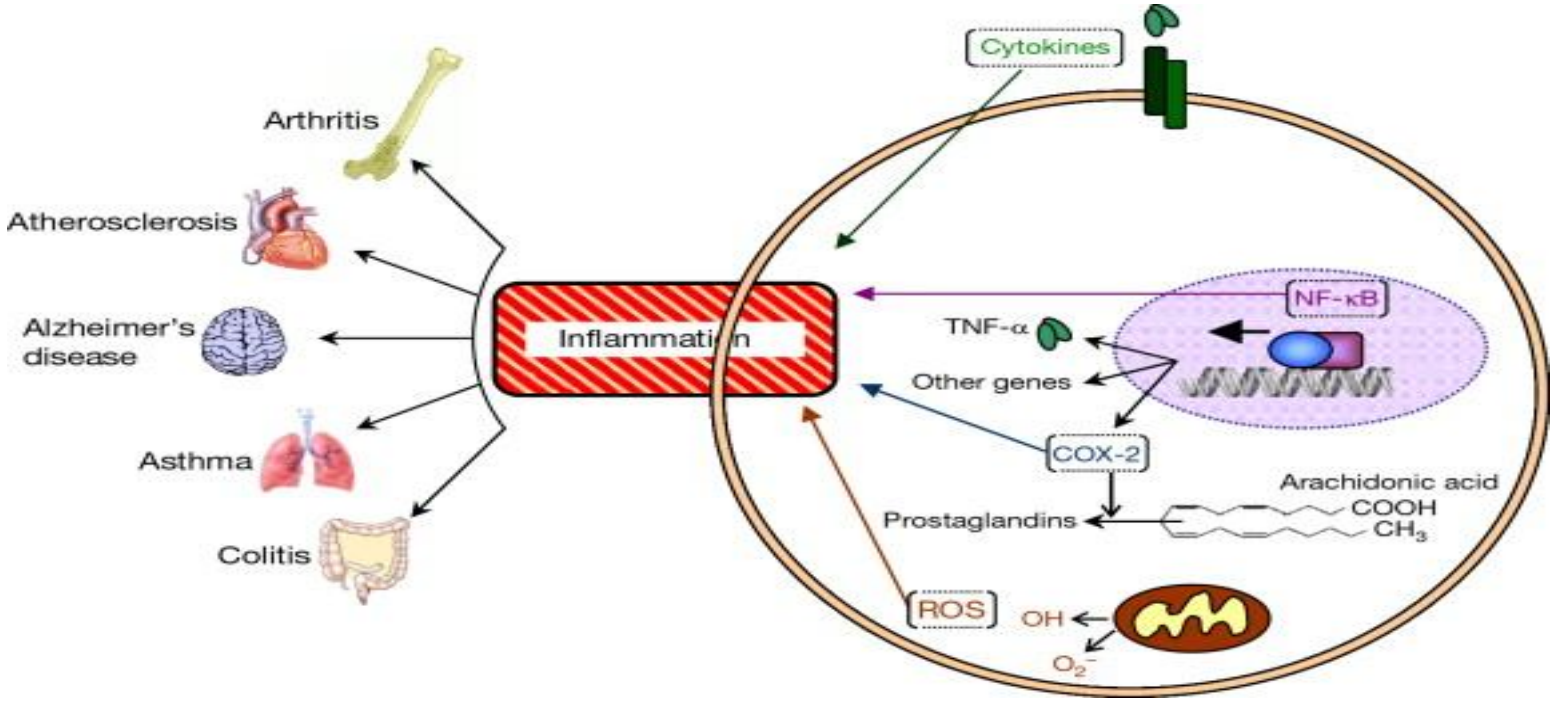
- The fructose molecules in the HFCS sweetener are free and unbound, ready for absorption and utilization. In contrast, every fructose molecule in sucrose that comes from cane sugar or beet sugar is bound to a corresponding glucose molecule and must go through an extra metabolic step before it can be utilized.
- The two components of sucrose are metabolized differently .

Hepatic Glucose and Fructose Metabolism After a Meal




W-6
Diet
W 3
Cis-LA, 18:2
α-ALA, 18:3
Δ6 Desaturase
(-)
(+)
GLA, 18:3
Glucose
Sucrose
Fructose
Insulin
DGLA, 20:3
(-)
(+)
PGs of 1 series
Δ5 Desaturase
AA, 20:4
EPA, 20:5
DHA, 22:6
Nitrolipids
Glucose
Sucrose
Fructose
PGs of 2 series, TXs,
LTs of 4 series
PGs of 3 series, TXs,
LTs of 5 series
(-)
(-)
(-)
Lipoxins
Resolvins
Protectins (NPDs)
eNO
Proinflammatory in
Nature
Anti-inflammatory in
Nature
Glucose
Sucrose
Fructose
(+)
ROS
(-)
Glucose
Sucrose
Fructose
Proinflammatory Cytokines
IL-6, TNF-α, HMGB1
Anti-inflammatory Cytokines
IL-4, IL-10, IL-12
Institution of Inflammation
Resolution of Inflammation

Scheme showing the metabolism of essential fatty acids; their role in inflammation; and the effect of glucose, sucrose, and fructose on the activities of desaturases and formation of various eicosanoids, cytokines, and lipoxins, resolvins, and protectins. (þ) Indicates increase in the activity or enhanced formation. () Indicates decrease in the activity or decreased formation. Glucose, sucrose, and fructose may decrease the activities of D6 and D5 desaturases and thus, decrease the formation of AA, EPA, and DHA that are precursors of various eicosanoids and lipoxins, resolvins, and protectins. Glucose, sucrose, and fructose seem to enhance the formation of proinflammatory prostaglandins, leukotrienes, and thromboxanes and decrease the formation of lipoxins, resolvins, and protectins that have anti-inflammatory activities and prevent development of type 2 diabetes mellitus, metabolic syndrome, and insulin resistance; they also may enhance the formation of proinflammatory cytokines and decrease those of antiinflammatory cytokines. The proinflammatory activities of glucose, fructose, and sucrose may be in the order of fructose.

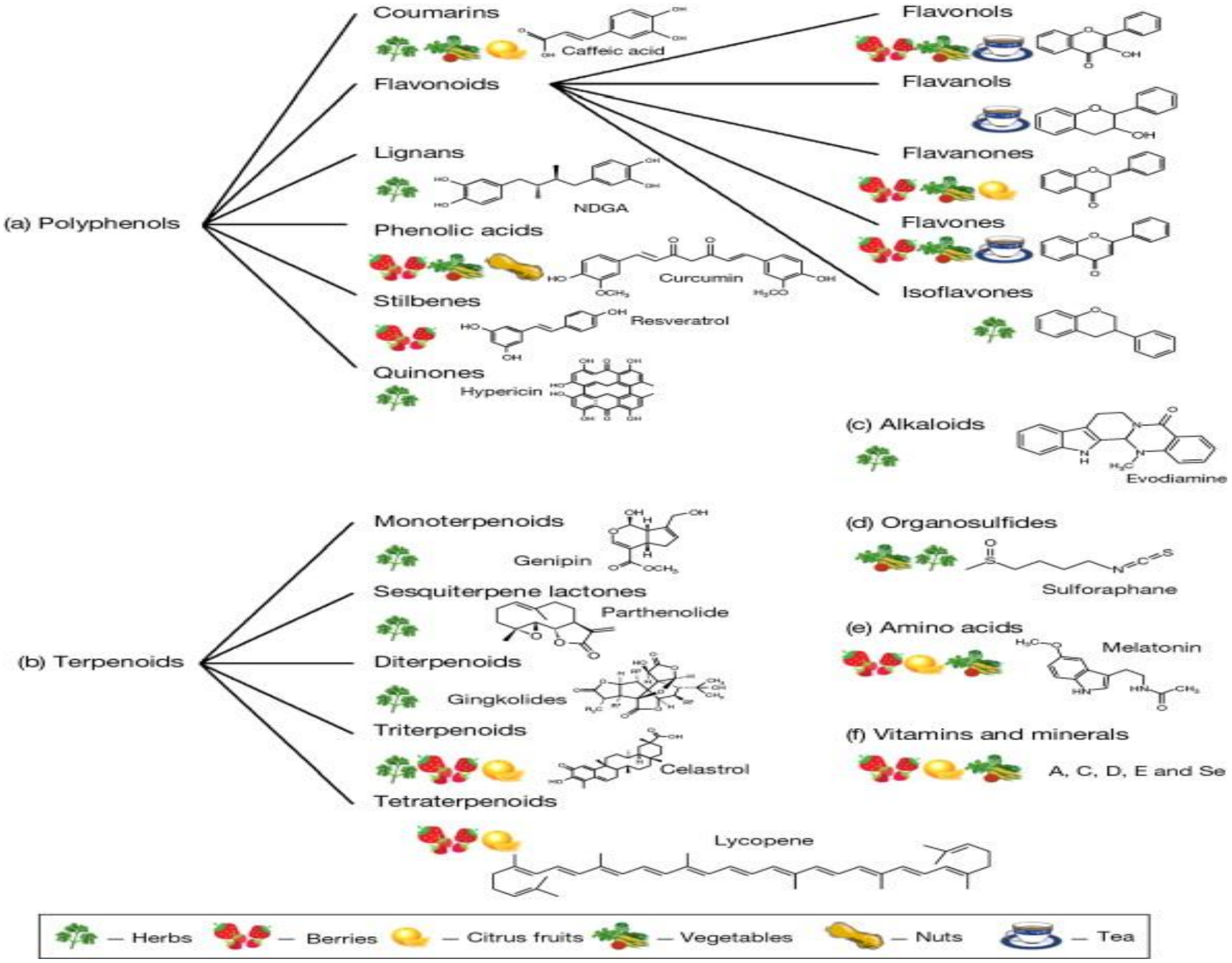


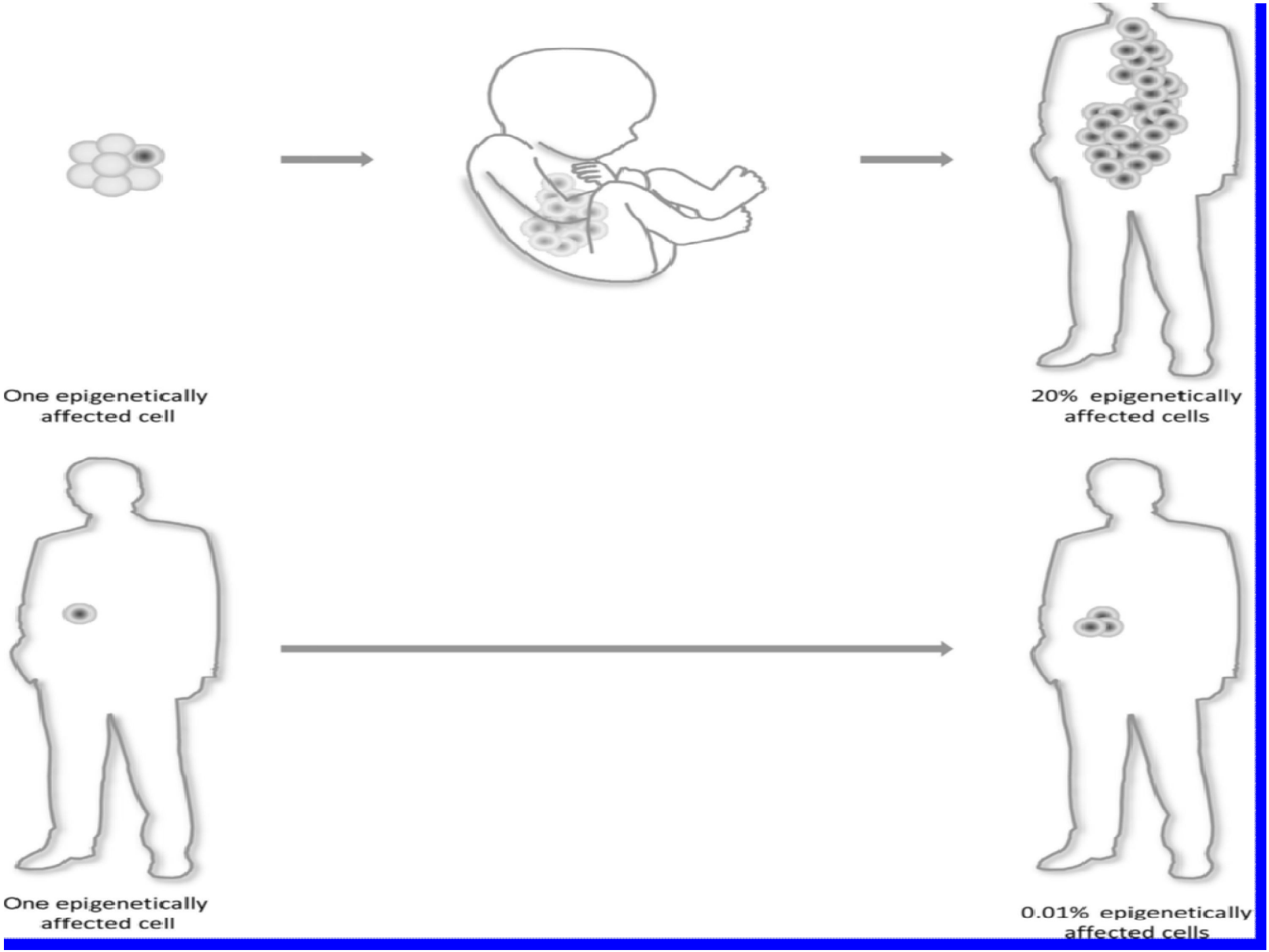
Molecular events that contribute to inflammatory process manifesting pathology in various disease modalities. Development of inflammation is a multilayered process involving interconnected cellular factors. As extrinsic signals, cytokines induc...

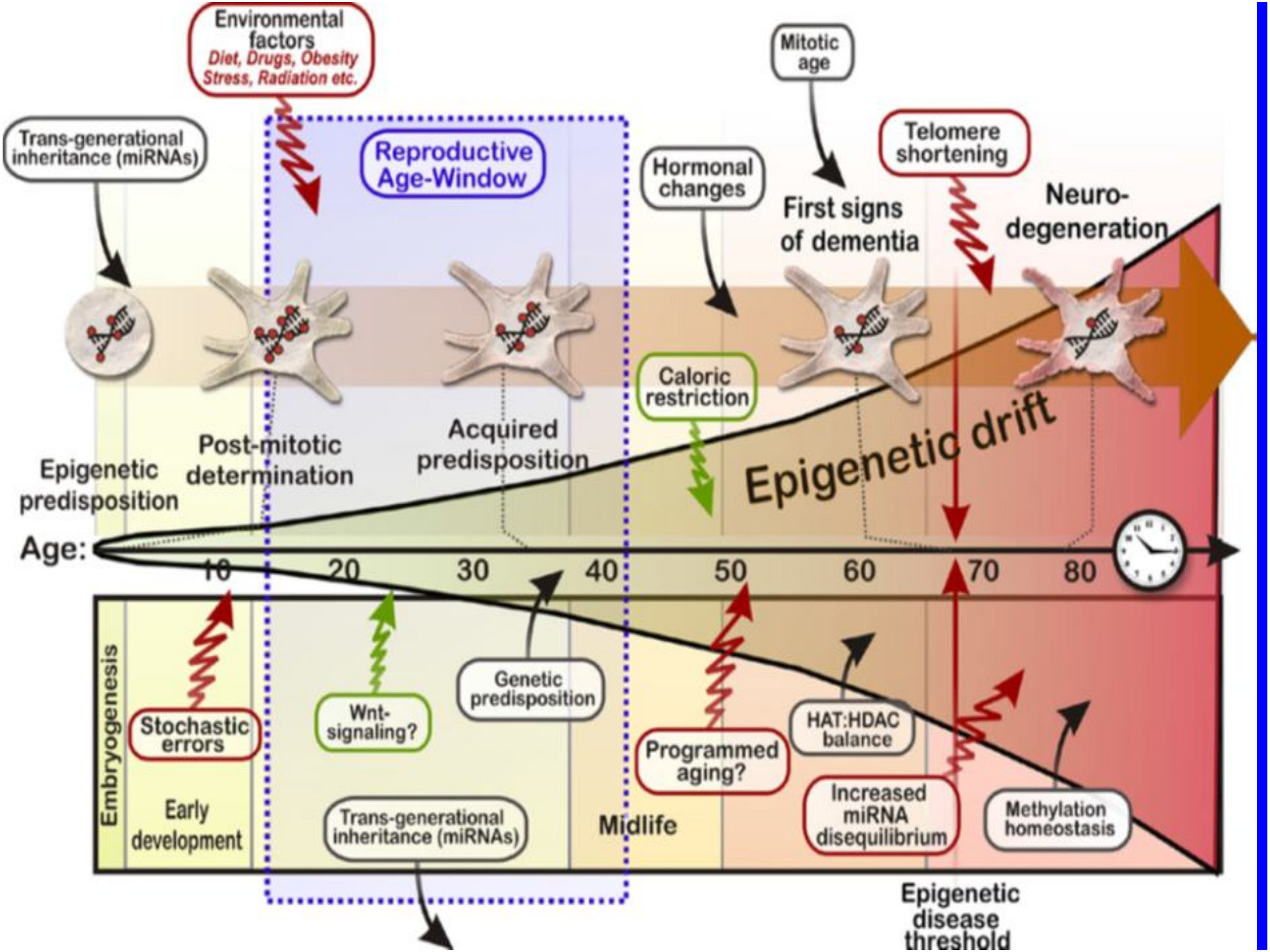
H.K. Prabhala , C. Pai , R.H. Prabhala

Chapter 21 - Anti-Inflammatory Natural Foods

Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases


(a) Polyphenols
Coumarins
Caffeic acid
Flavonoids
Lignans
NDGA
Phenolic acids
Curcumin
Stilbenes
Resveratrol
Quinones
Hypericin
Flavonols
Flavanols
Flavanones
Flavones
Isoflavones
(c) Alkaloids
Evodiamine
(b) Terpenoids
Monoterpenoids
Genipin
Sesquiterpene lactones
Parthenolide
Diterpenoids
Gingkolides
Triterpenoids
Celastrol
Tetraterpenoids
Lycopene
(d) Organosulfides
Sulforaphane
(e) Amino acids
Melatonin
(f) Vitamins and minerals
A, C, D, E and Se
— Herbs
— Berries
— Citrus fruits
— Vegetables
— Nuts
— Tea


One epigenetically affected cell
20% epigenetically affected cells
One epigenetically affected cell
0.01% epigenetically affected cells


Environmental factors
Diet, Drugs, Obesity
Stress, Radiation etc.
Mitotic age
Trans-generational inheritance (miRNAs)
Reproductive Age-Window
Hormonal changes
Telomere shortening
First signs of dementia
Neuro-degeneration
Caloric restriction
Epigenetic predisposition
Post-mitotic determination
Acquired predisposition
Epigenetic drift
Age:
10
20
30
40
50
60
70
80
Embryogenesis
Early development
Stochastic errors
Wnt-signaling?
Genetic predisposition
Programmed aging?
HAT:HDAC balance
Increased miRNA disequilibrium
Methylation homeostasis
Trans-generational inheritance (miRNAs)
Midlife
Epigenetic disease threshold

Alzheimer's Disease

- Poorly Understood Neurological Disorder
- Many Potential Therapies but No Acceptable Drug
- Current Approach – Poly-Pharmacy
  - Memory Decline
  - Behavioural Changes
  - Functional Decline
  - Related or Concomitant Pathologies

Experimental Strategies for the Pharmacological Treatment of Alzheimer's Disease

-
- New Cholinesterase Inhibitors
- Cholinergic Receptor Agonists
- Monoamine Regulators
- Antioxidants and Immunotherapy
- Diverse Natural Compounds, Extracts and Phytomedicines Derived from Plant Sources with Poorly Understood Mechanism of Action

Herbal Medicinal Products with Potential for Treatment of AD

- Alkaloids from the Calabar bean (*Physostigma vene-nosum*)
- Huperzine A from *Huperzia serrata*
- Galantamine from the snowdrop *Galanthus woronowii*
- Cannabinoids (cannabidiol) from *Cannabis sativa*
- Saffron (*Crocus sativus*)
- Ginseng (*Panax species*)
- Sage (*Salvia species*)
- Lemon balm (*Melissa officinalis*)
- *Polygala tenuifolia*

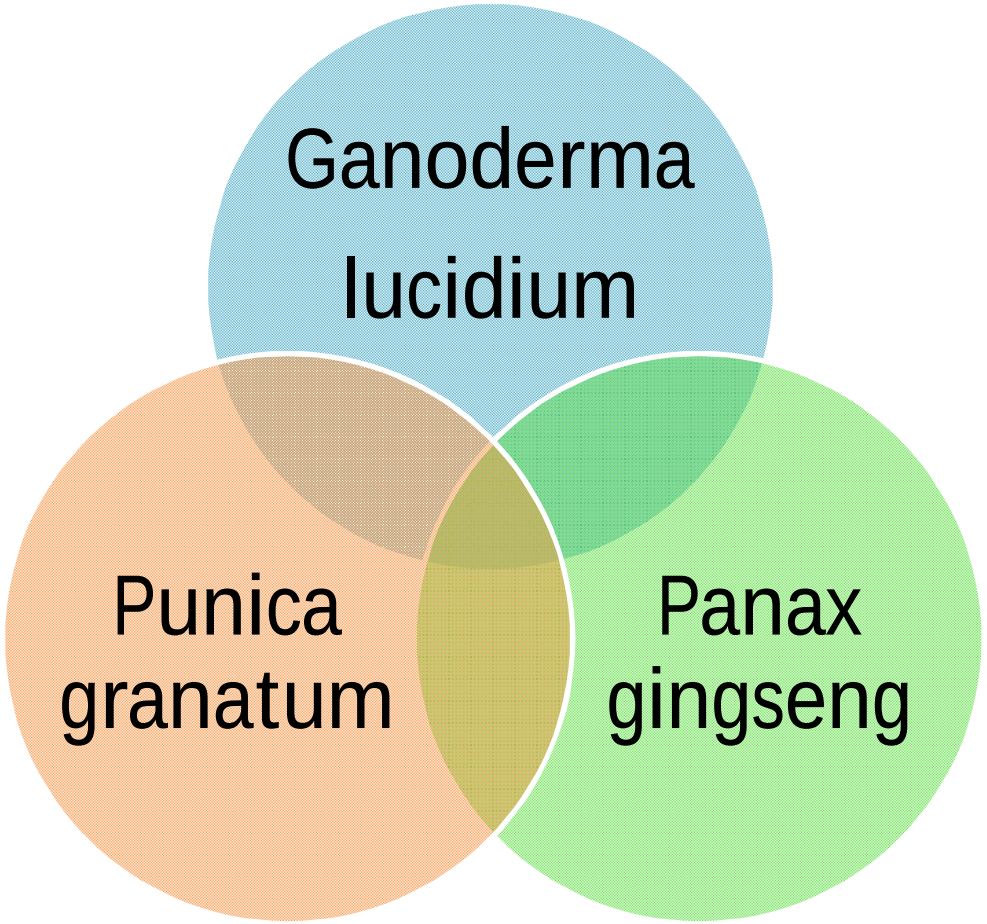
Herbal Med. Products with Potential for Treatment of AD -3

- Drumstick tree (*Moringa oleifera*)
- Phytoestrogens
- Walnut extract
- *Erigeron annuus* leaf extracts
- Epigallocatechin-3-gallate
- Luteolin
- The brown algae (*Ecklonia cava*)
- Gami-Chunghyuldan (standardized multiherbal medici-nal formula)
- *Punica granatum* extracts
- Ginkgo/Maidenhair tree (*Ginkgo biloba*)
- Sicklepod (*Cassia obtisufolia*)
- Sal Leaved Desmodium (*Desmodium gangeticum*)
- Lemon Balm (*Melissa officinalis*)
- Garden sage, common sage (*Salvia officinalis*)

IMMUNOVIT –IHP

HELP YOUR BODY FIGHT DISEASES.

IMMUNOVIT-IHP



IHP-VIRGIN COCONUT OIL (VCO)

- " Approximately 50% of the fatty acid in coconut are lauric acid. LA is MCFA which when converted into monolaurin in human and animals body possesses antiviral, antibacterial, antifungal, antiprotozoal monoglyceride used by man to destroy lipid coated viruses such as HIV. . . . "**Dr. Mary Enig. a PHD Nutritionist/Biochemist and one of the world's leading authorities on fats and oils.**

IHP-VIRGIN COCONUT OIL (VCO)

Okra
Abelmoschus esculentus Moench

- Okra mucilage has been used as a plasma replacement. The mucilage in okra binds cholesterol and bile acids that are carrying toxins produced by the liver.

- Anti-oxidant, rich in minerals and vitamins

Tomatoes

Solanum lycopersicum

- Lycopene and b -carotene are the tomato carotenes which present the highest nutritional value. Specifically, lycopene reduces several cancer types and the risk of heart attack.
- It is useful in preventing prostrate enlargement

OGBONO

Irvingia gabonensis

- Weight loss remedy in Europe and America – as African Bush Mango

OGBONO - Irvingia

- Highest selling anti-obesity medicine
- Differentiation between ‘ado’ and ‘ugiri’ varieties?

Mucuna pruriens

- Male Erectile Dysfunction
- Parkinson's Disease Management

Dawa-Dawa – *Parkia biglobosa*

- Seeds are antioxidant antihypertensive
- Leaves are antihypertensive
- Fermented seeds used as soup flavoring agent

Tumeric - *Curcuma longa*

- Arthritis
- Inflammation
- Antidepressant
- Immune Stimulant
- Antioxidant
- Gastro System Dysfunction

Ugu – *Telfairia occidentalis*

Baobab - *Adansonia digitata*

- Analgesic, antiinflammatory
- Anttviral
- Antioxidant
- Energy drink
- Rich in vitamins and minerals
- Cosmetics

Guinea Corn - *Sorghum bicolor*

- Highly Nutritious – Rich in proteins and amino acids
- Two proprietary products for sickle-cell anemia are based on the chelation of the sheath poly-phenols with suitable metal.
- Phyto-Erythropoetin -K

Moringa oleifera

Nigerian Fruit Diversity – Potential Health Drinks

ACKNOWLEDGEMENTS

- Prof. Elijah Sokomba
- Dr. Chris Okunji and the U.S. team
- Dr. Michel Tchimene & InterCEDD staff
- Ann Ijeoma Nwafor, M.Sc.
- Chinyere Douglas, M.A.
- Paschal Okwara
- Pharm. Joseph Abimaje Iduh
- Amu Omoikhudu

ACKNOWLEDGMENTS - 2

- **Ijeoma, Benson O. - M.Sc.**
- Richard Imah
- Mildred Udeagbala
- Ugochi Uwandu
- Members of the Scientific Advisory Committee
- And all the staff of Bioresources Development Group

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Thank You !!!