Systemic Enzyme Therapy (SET)

Types of Enzymes

- **digestive enzymes -** source of nutrients (lipids, sugars, proteins) : ptyalin, pepsin, trypsin, lipase, protease, amylase
- **metabolic enzymes –** energy source, detox.
- **food enzymes** in raw food, enzyme suppl.

Healthy body´s enzyme supply versus insufficient enzyme production in pathological states.

Systemic Enzyme Therapy

- therapeutic method with the use of the combined enzyme preparations to treat inflammatory diseases
- also called Systemic Enzyme Support

ATC classification: Enzymes M09AB

Effects of systemic enzyme formulations

- immunomodulatory
- anti-inflammatory
- anti-edematic
- analgesic
- fibrinolytic
- thrombolysis
- anti-tumor
- antioxidant properties

Indications:
- inflammatory diseases
- lymphedema
- sport injuries
- recurrent infections
- radiotherapy

Systemic enzyme therapy

- designed in Germany in the 1960s
- dr. Max Wolf and Helen Benitez (Wobenzym)
- proteolytic enzyme theory
- evaluation of enzymes of the plant and animal origin
- studies of enzyme interactions (dr. Ransberger)

Systemic enzyme formulations

CONSTITUENTS

- **pancreatin** - combination of proteolytic enzymes
- **bromelain** - a cysteine endopeptidase
- **papain** - similar actions as bromelain
- **trypsin** - serine endoprotease, protein/amino acid metabolism
- **chymotrypsin** - amino acid metabolism
- **amylase** - converts starch to sugar
- **lipase**

other constituents:
- **rutin** – bioflavonoid, strengthening the walls of capillaries, scavenger (a glycoside form of quercetin, from Sophora japonica)
- **thymus extract**

Systemic enzyme therapy

PHARMACODYNAMICS OF SYSTEMIC ENZYMES

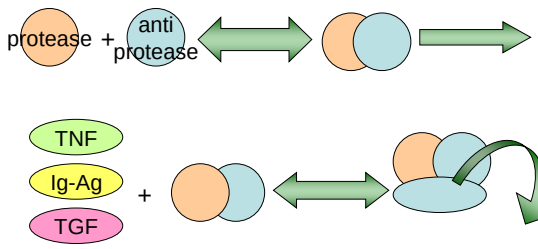
- **alpha 2-macroglobulin (a2M) activation**
  - a serum binding, carrier, and targeting protein, facilitates the binding and removal of foreign peptides, excessive inflammatory mediators and auto-toxic endogenous proteins

Effects on inflammatory proceses

- enhancing the proteolytic activity of the blood
- antiaggregatory and fibrinolytic effect
- immunomodulatory effect – influence on the cytokine spectrum

Systemic enzyme therapy

PHARMACODYNAMICS AND PHARMACOKINETICS OF SYSTEMIC ENZYMES



Systemic enzyme therapy

PHARMACODYNAMICS AND PHARMACOKINETICS OF SYSTEMIC ENZYMES

- proteases are bound with antiprotease enzymes to form complexes in the blood circulation:

specific: alpha 1- antitrypsine
alpha 1- antichymotrypsine

non-specific: alpha 2 – macroglobulin
it binds host or foreign peptides and particles, thereby serving as humoral defense barriers against pathogens in the plasma and tissues

Systemic enzyme therapy

PHARMACODYNAMICS AND PHARMACOKINETICS OF SYSTEMIC ENZYMES

Systemic effect
Resorption from the lumen of the intestine 10 %
Bioavailability 1 %

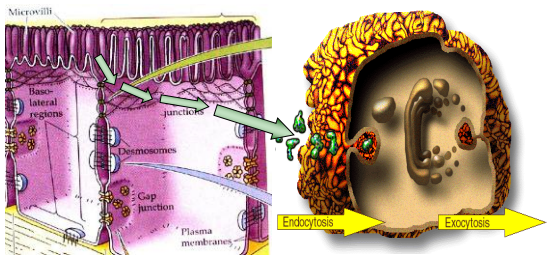
- high doses needed

- orally on empty stomach
- swallowed without chewing
- at least 30 minutes before meal,
- 2 hours after the last meal
- with a glass of water (250 ml and more)

Systemic enzyme therapy

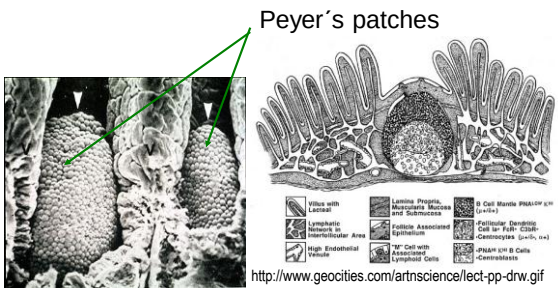
PHARMACOKINETICS OF SYSTEMIC ENZYMES

endocytosis -> exocytosis



Systemic enzyme therapy

PHARMACOKINETICS OF SYSTEMIC ENZYMES



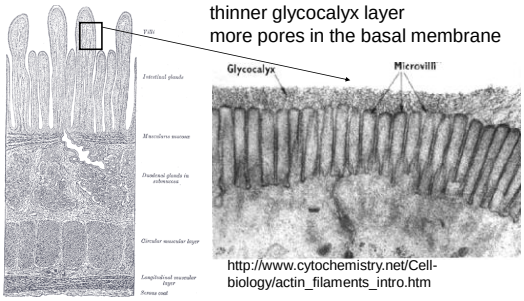
http://www.geocities.com/artnscience/lect-pp-drw.gif

Systemic enzyme therapy

PHARMACOKINETICS OF SYSTEMIC ENZYMES

absorption

ileum, distal part of the small intestine
thinner glycocalyx layer
more pores in the basal membrane



http://www.cytochemistry.net/Cell-biology/actin_filaments_intro.htm

Systemic enzyme therapy

PHARMACOKINETICS OF SYSTEMIC ENZYMES

Non-resorbed enzymes are

excreted by the faeces

degradated by the metabolism

Systemic enzyme therapy

Enzyme combinations
- increased resorption
- increased effect

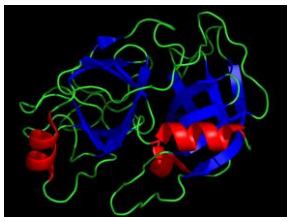
Enzymes from animals	Enzymes from plants
Trypsin	Bromelain
Chymotrypsin	Papain
Pancreatin	

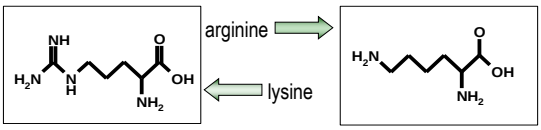
Systemic enzyme therapy

TRYPSIN

serin endopetidase
of the pancreatic origin

basic aminoacids



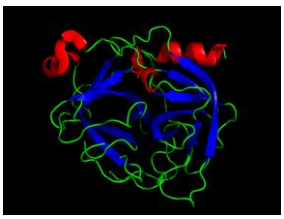


Systemic enzyme therapy

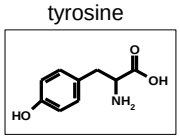
CHYMOTRYPSIN

endopetidase
of the pancreatic origin

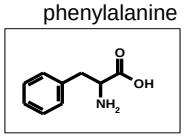
non-polar aminoacids



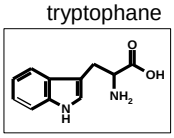
tyrosine



phenylalanine

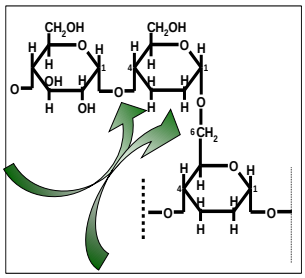


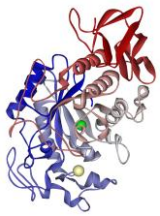
tryptophane



Systemic enzyme therapy

alpha - AMYLASE





hydrolase
of the pancreatic origin

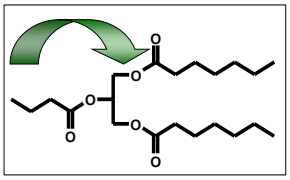
alpha-1,4- a 1,6 -
glycosidic bond

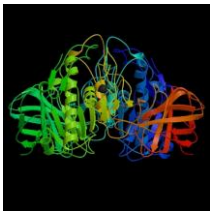
Systemic enzyme therapy

LIPASE

hydrolase of the pancreatic origin

primary ester binding of the TAG





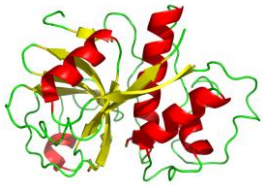
http://www.cs.stedwards.edu/chem/Chemistry/CHEM43/CHEM43/Lipases/pancreatic%20lipase.jpg

Systemic enzyme therapy

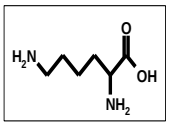
PAPAIN

mixture of proteases from unripe papaya fruits

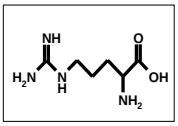
cleavage of the bonds of



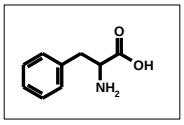
lysine



arginine



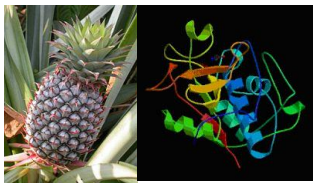
phenylalanine

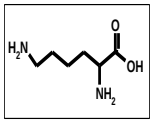


Systemic enzyme therapy

BROMELAIN

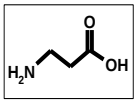
cysteine endopeptidase from the from the stemm of the pineapple plant (Ananas comosus)

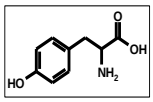




lysine

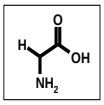
alanine





tyrosine

glycine



Systemic enzyme therapy

Side effects

- fibrinolytic effect - CAVE before surgery!
- flatulence, nausea
- allergic skin reactions
- changes in consistency of faeces

- may increase ATB plasma levels
- no MUTAGENESIS, no CARCINOGENESIS after longterm administration

Systemic enzyme therapy

Contraindications

- allergy
- blood clotting disorders
- peptic ulcer disease
- consideration in pregnancy and lactation
- ! increase ATB plasma levels

Systemic enzyme therapy

Clinical applications of SET

Andrology, Men's Health
Arthritis, Rheumatology
Osteoarthritis
Rheumatoid Diseases
Reactive arthritis
Fibromylagias

- Cardiology
- Dentistry
- Diabetology
- Hepatology

Immunology/Infectious Diseases
Lymphology
Nephrology
Neurology
Oncology
Otolaryngology
Pulmonology
Traumatology, Surgery
Urology
Vascular Medicine

by Joseph J. Collins, RN, ND

Systemic enzyme therapy
in immunopathological states

- support balanced humoral immune function and modulate systemic inflammation
- efficiency due to anti-inflammatory, anti-edema, analgesic, fibrinolytic, thrombolytic, anti-tumor and antioxidant properties
- protease activation of alpha2-macroglobulin modulates a chaperone-like action with broad specificity

Inflammatory mediators

Pro-inflammatory cytokines: TH1
- INFgamma, TNF alpha, IL-2, IL-6, IL-12

Anti-inflammatory cytokines: TH2
- IL-4, IL-5, IL-10, TGF-beta

- SET modulates systemic inflammation
- SET supports balanced humoral immune function
- SET (proteolytic enzymes) facilitate the removal of excessive mediators of inflammation: foreign peptides, inflammatory mediators and auto-toxic endogenous proteins

Biomarkers of inflammation

- increased erythrocyte sedimentation rate (ESR)
- increased C-reactive protein (CRP)
- abnormal immunoglobulins levels (IgG, IgE, IgA,IgM)
- increased circulating immune complexes (CIC)
- increased cytokine production with an imbalance of cytokines
- increased fibrin activation and fibrosis
- increased amyloid production and deposition in neuro-degenerative diseases
- damaged proteins and cellular debris in aging

Systemic enzyme therapy
in immunopathological states

- **decrease of ESR levels** in relapsing urinary tract infections, adnexitis, and acute trauma
- **lower CRP levels** in rheumatoid arthritis and acute trauma
- **decrease of CRP levels** in lymphedema patients
- **decreased CIC levels** when used as an adjuvant (with methotrexate) in rheumatoid arthritis
- decreased excessive pro-inflammatory cytokines (IL-1b and TNF-alpha) in RA patients
- **increased blood fibrinolytic activity and proteolysis** of extravascularly deposited fibrin

Systemic enzyme therapy
in neurodegenerative diseases

- alpha2-macroglobulin associates with b-amyloid peptide and prevents fibril formation
- degradation of amyloid beta-protein by a serine protease-alpha-2-macroglobulin complex
- distinct binding sites in the structure of alpha 2-macroglobulin mediate the interaction with beta-amyloid peptide and growth factors