

# ASPIRIN

What history learns  
about  
the future

Gert Laekeman  
Salicaceae Symposium  
Meise Botanical Garden  
25<sup>th</sup> May 2019





MIRRE GOMHARS









# CARDIOASPIRINE®

100 mg maagsapésistente tabletten - Acetylsalicylzuur

Maagsapésistente tabletten



## ASAFLOW®

## 80 mg

Acetylsalicylzuur/Acetylsalicylsäure



Traitement et prévention des affections cardiovasculaires  
Behandeling en preventie van cardiovasculaire aandoeningen  
Behandlung und Vorbeugung von kardiovaskulären Leiden







bron: <http://www.kuleuven-kulak.be/bioweb/>





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# Edwin Smith 1858

*... if you examine a man ....*  
48 cases

Ebers' papyrus scrolls  
    < 3000 Vc

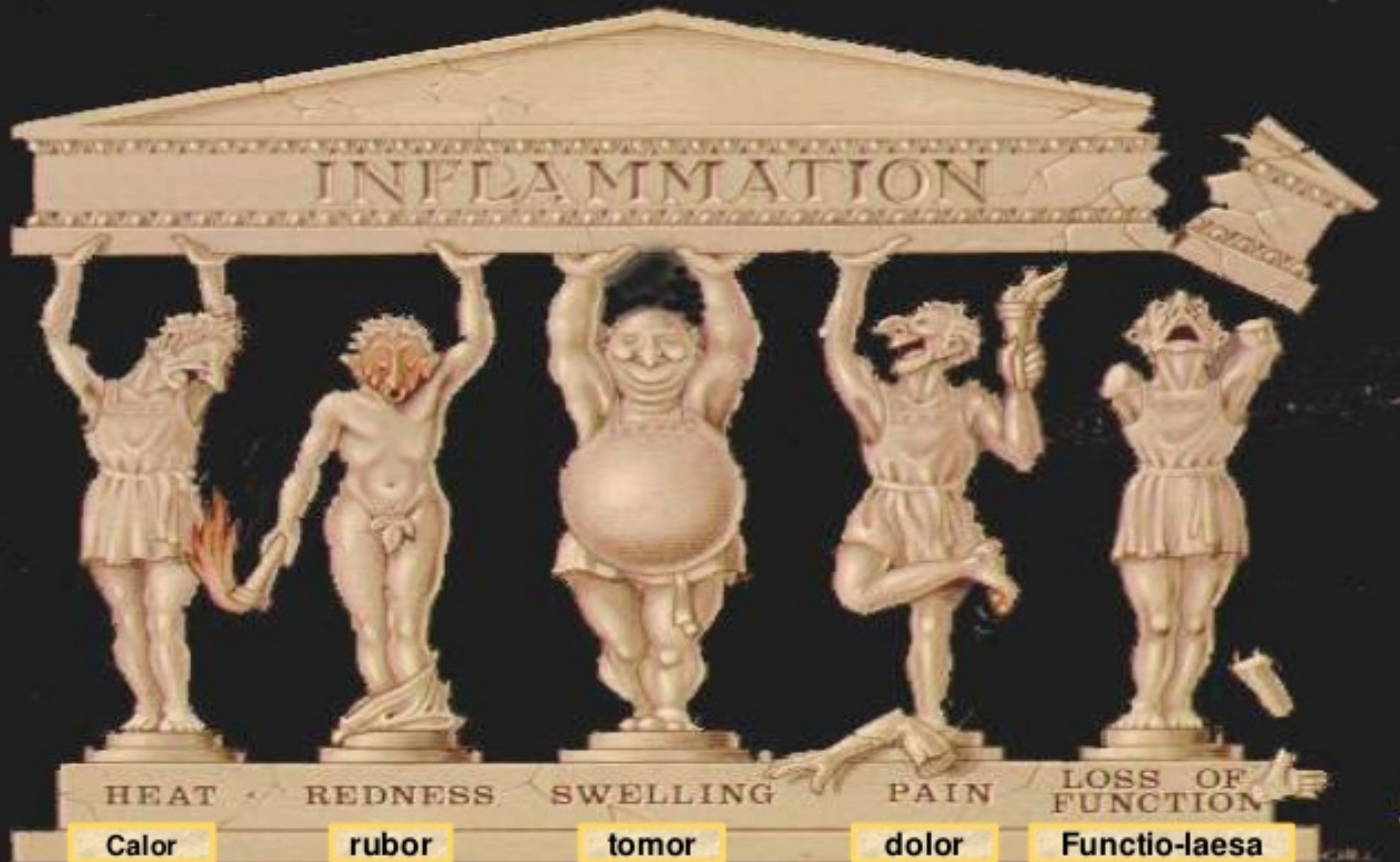
± 160 medicinal herbs

a.o. onion, water melon, juniper,  
cinamon, anis seed, date, celeri and  
... willow





# Cardinal signs of inflammation





# Greece - Rome

Based on Egyptian tradition

Hippocrates (5<sup>th</sup> century BC): pain / fever

Celsus (AD 30): 4 symptoms of inflammation

Rubor, calor, dolor, tumor

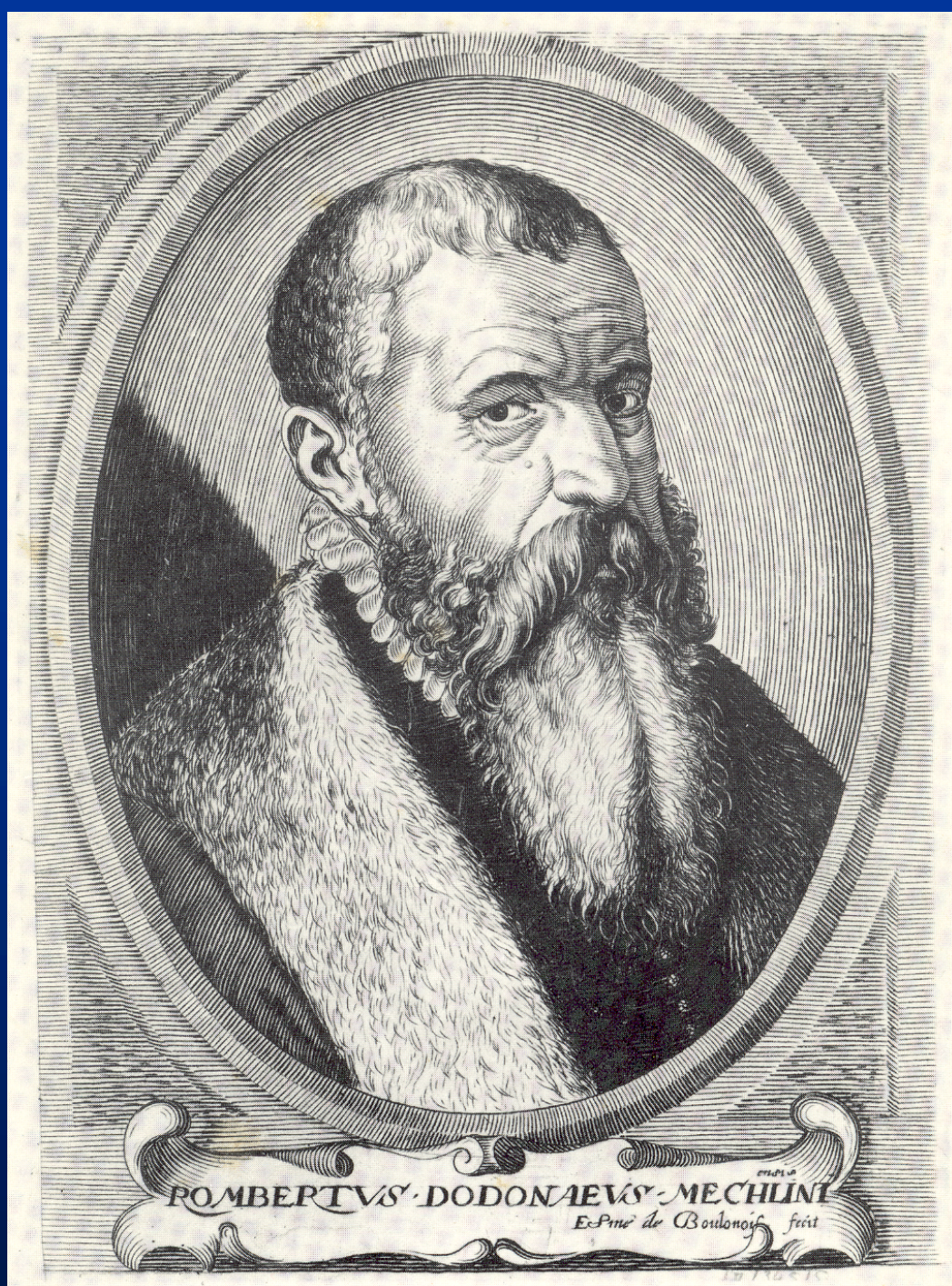
Dioscorides under Nero Emperor

Plinius the Old: 37 volumes *Naturae Historia*

Galenus (AD 216): willow bark = basic medicine







Rembert Dodoens  
Mechelen > 1517

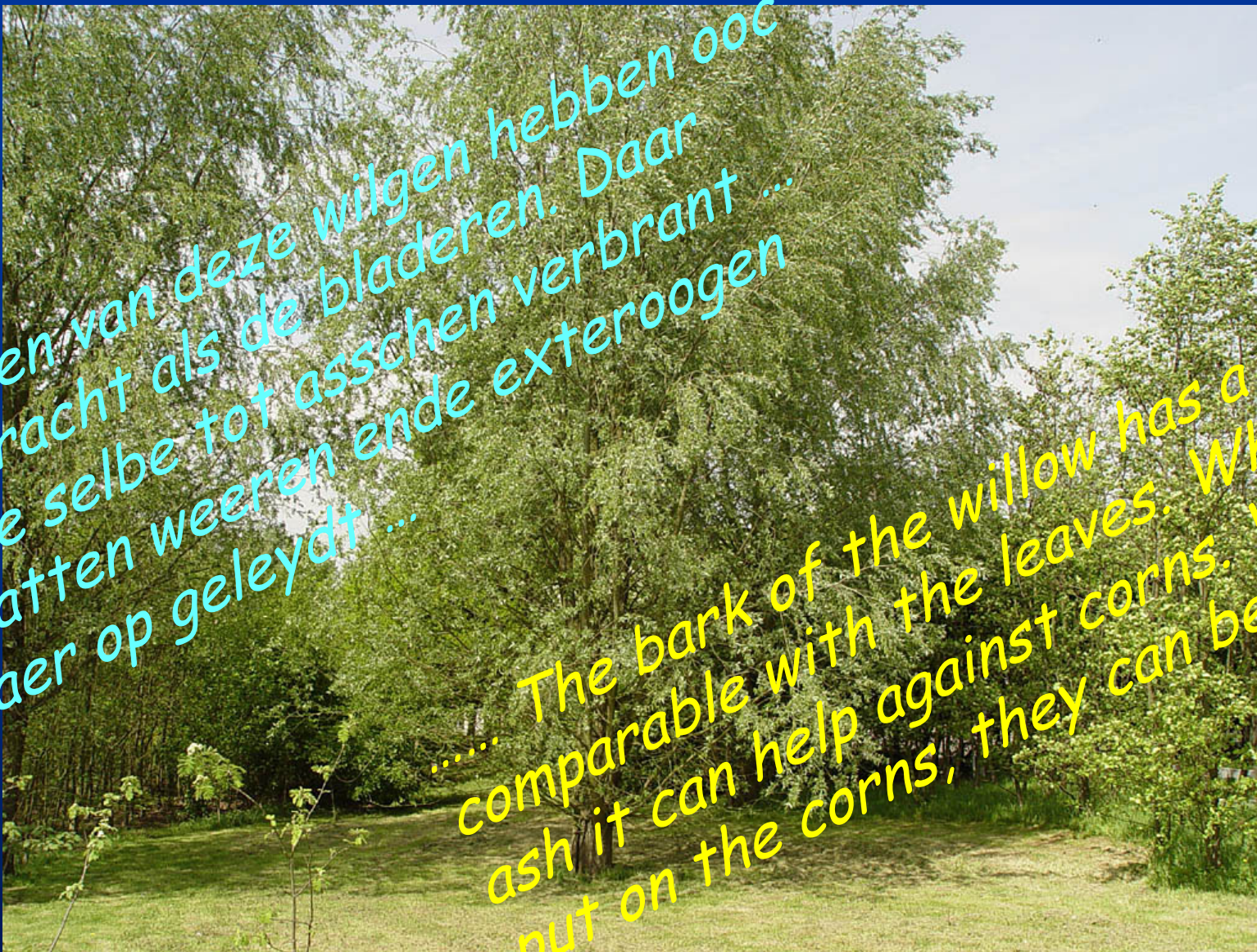
Rembertus Dodoneus  
Leiden



# Willow according to DODOENS

..... De schorssen van deze wilgen hebben ooc  
diergelycke cracht als de bladeren. Daar  
benedeffens de selbe tot asschen verbrant ...  
doen de wratten weeren ende exteroogen  
afvallen daer op geleydt ...

..... The bark of the willow has a power  
comparable with the leaves. When heated to  
ash it can help against corns. When the ash is  
put on the corns, they can be removed ...







Chipping Norton



# Reverend Edward Stone - Chipping Norton

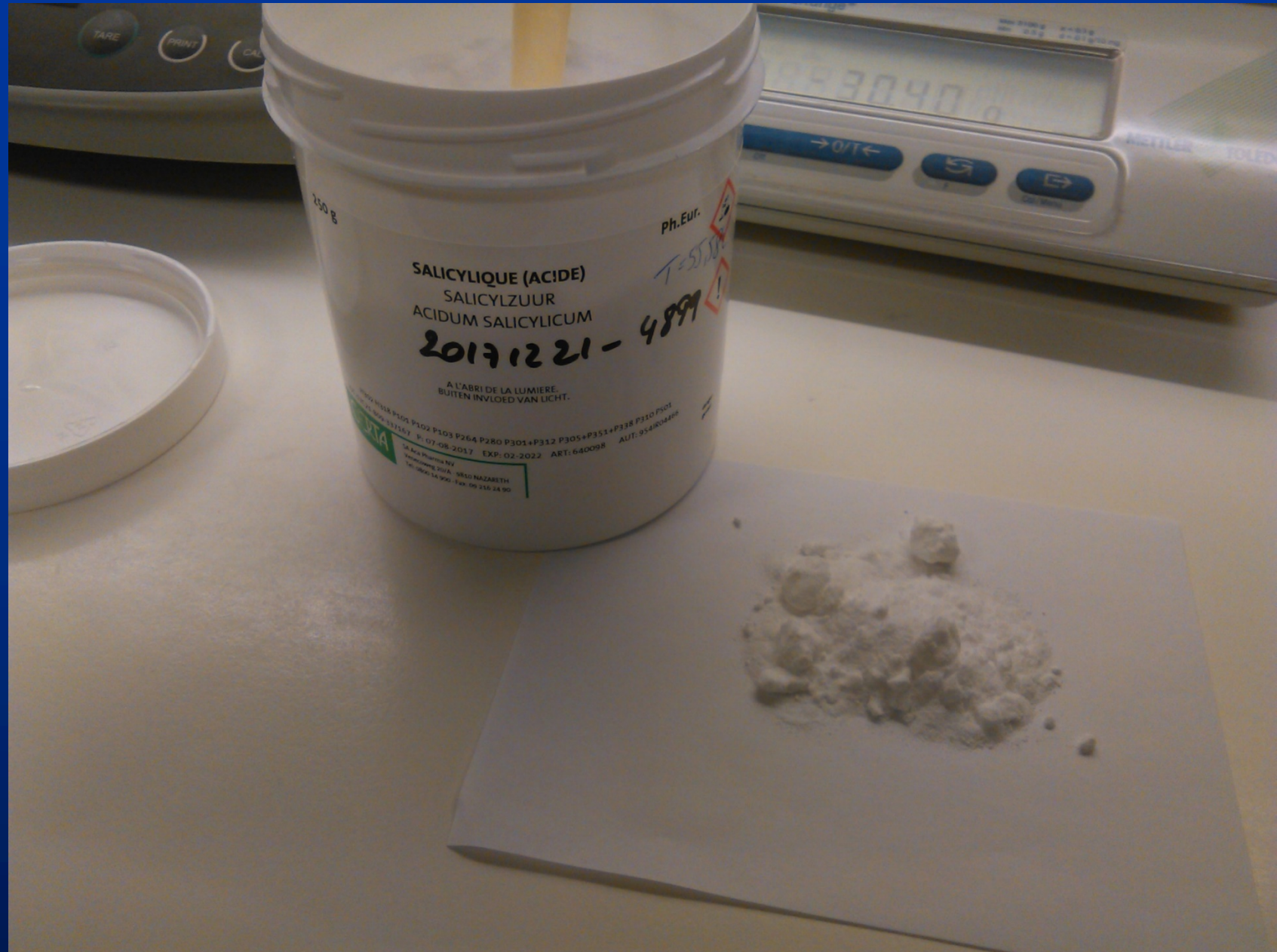
## 1ste helft 18de eeuw

*There is a bark of an English tree, which I have found by experience to be a powerful astringent and very efficacious in curing **agues** and **intermitting disorders**. About six years ago, I accidentally tasted it, and was surprised at its extraordinary **bitterness**; which immediately raised in me a suspicion of its having the properties of the **Peruvian bark**. As this tree delights in a moist or wet soil, where agues chiefly abound, the general maxim, **that many natural maladies carry their cures along with them, or that their remedies lie not far from their causes**, was so very apposite to this particular case, that I could not help applying it, and that this might be intention of providence.*



# Raffaele PIRIA Italië 1838

Isolation of salicylic  
acid = stronger than  
extracts





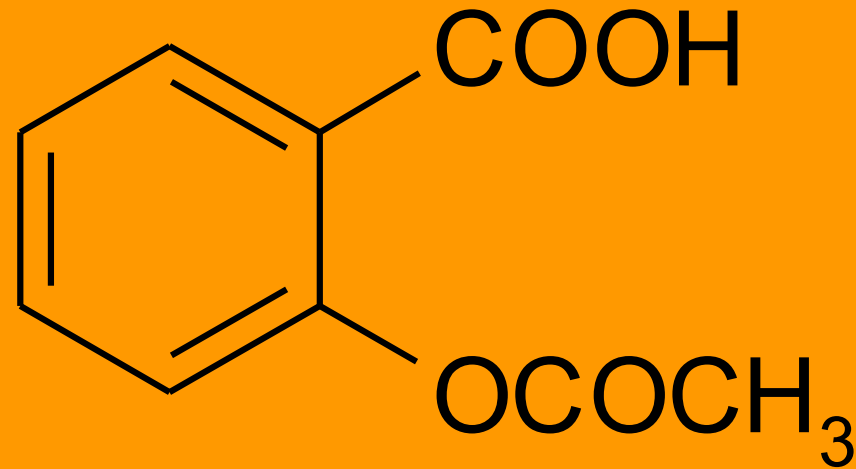
Johann PAGENSTECHER  
Berner-Oberland (CH)  
Karl Jacob LÖWIG  
Berlijn  
> 1830

Filipendula ulmaria =  
meadowsweet  
Liquid preparation =  
tincture  
Löwig: spirsäure  
= painkiller  
Salicylic acid





# Charles Gerhardt 1853 Montpellier







# DAS DEUTSCHE REICH 1871-1918



Otto von Bismarck (Franz von Lenbach, 1890)





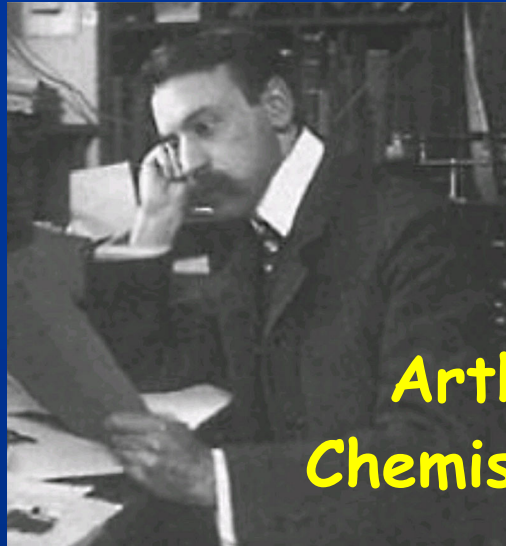
## Felix Hoffman Synthesis

Felix Hoffman

*... When salicylic acid (100,0 parts) is heated with acetic anhydride (150,0 parts) for 3 hours under reflux, the salicylic acid is quantitatively acetylated. After distilling off the acetic acid one obtains the above in the form of needles, which, when cristallized from benzene, melt at 136 degrees. In contrast with the literature reports, my acetyl product no longer gives a reaction with ferric chloride, which readily distinguished it from salicylic acid. By its physical properties, e.g. its sour taste without being corrosive, the acetylsalicylic acid differs favourably from salicylic acid, and is now being tested in this respect for its usefullness ...*

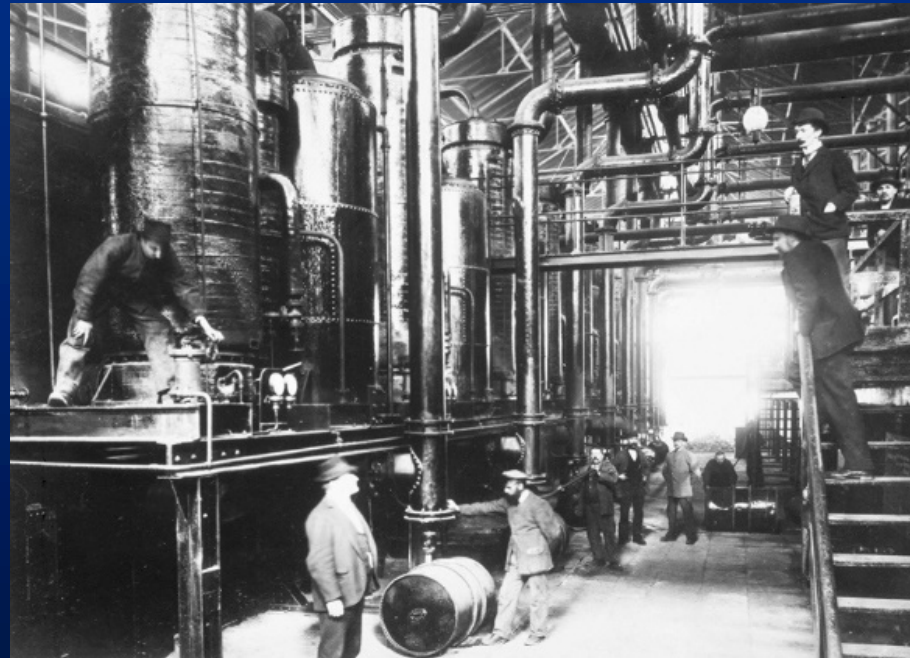
10 August 1897 (laboratory diary)





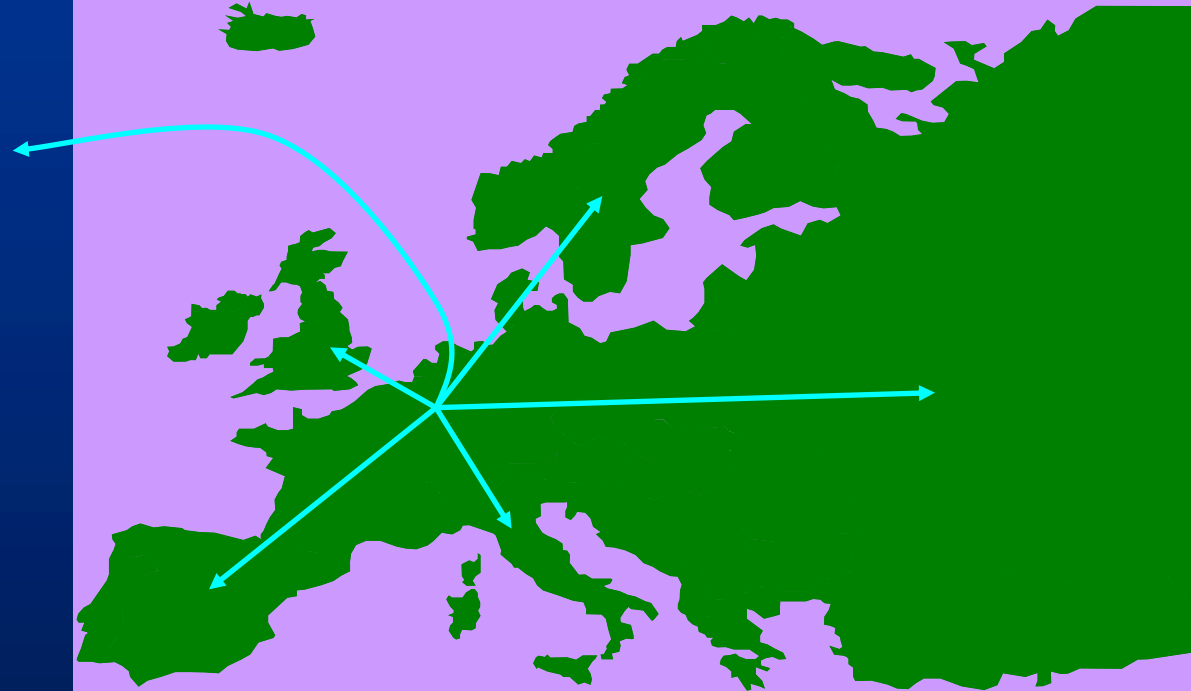
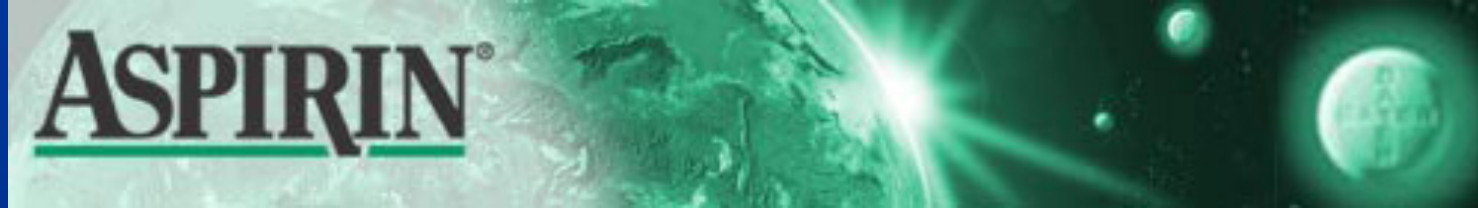
Arthur Eichengrün  
Chemistry department

Heinrich Dreser  
Pharmacology department





1899







**1956**  
**St.-Louis - Missouri**  
**Monsanto Chemical Company**

100 millionth pound of aspirin

Carroll A. Hochwalt (Monsanto R&D)

*... There is still much to be learned of the compound's mechanism of action. How does it do what it does for the rheumatic and arthritis sufferers? Why does it reduce abnormal body temperatures while having no effect on normal temperatures? Just what is the means by which aspirin succeeds in moderating pain? The answers to these and other questions are sure to come in time and with them may come still more important applications for this cheapest, safest and most perennially durable of the genuine wonder drugs ...*



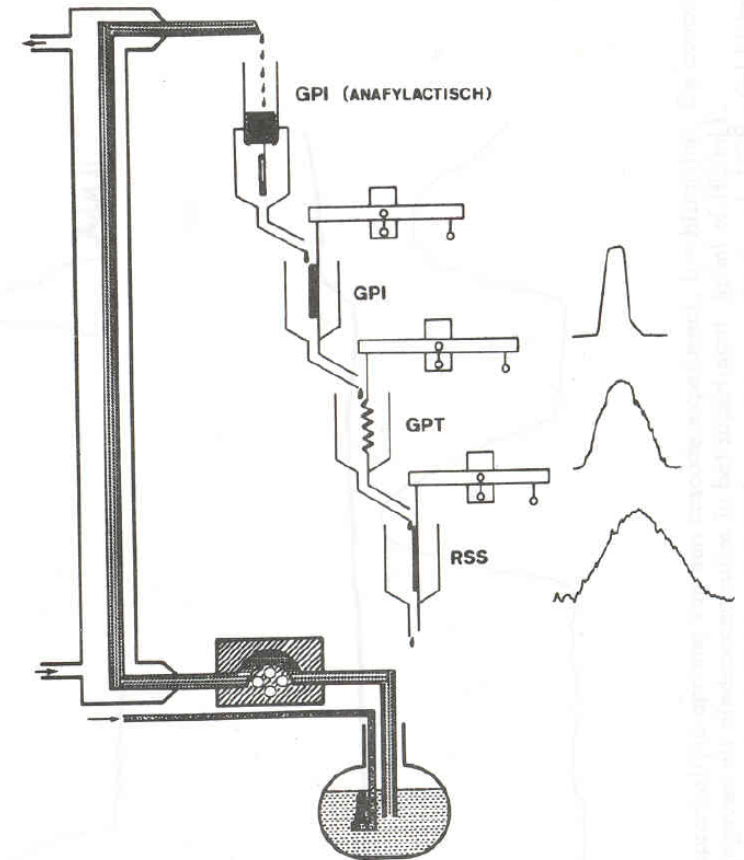


# John R. Vane 1971

Guinea-pig  
lung

Rabbit aorta  
RCS

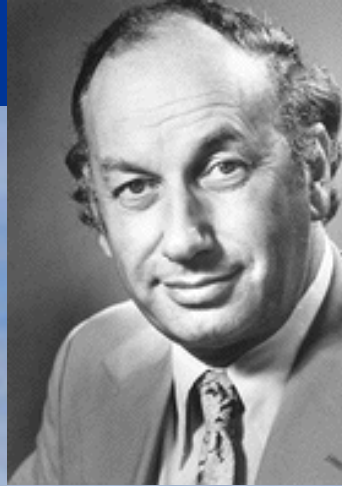
'Cascade'



Vane, JR: Inhibition of Prostaglandin  
Synthesis as a Mechanism of Action  
of Aspirin-like Drugs.  
*Nature, New Biology*, 231:323, 1971.



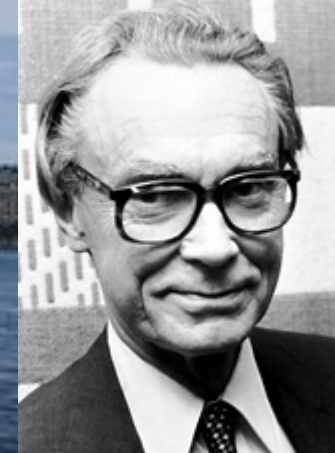
# NOBELPRICE 1982



Sr. John R. Vane 1927-2004



Bengt I. Samuelsson 1934



Sune K. Bergström 1916-2004

**ASAFLOW<sup>®</sup>** 80 mg

Acetylsalicylzuur/Acetylsalicylsäure



2542488174766802



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## Take home messages

- Importance of history
- Importance of natural resources
- Importance of observation
- Importance of rational thinking
- Importance of patience
- Importance of simplicity