4GENE

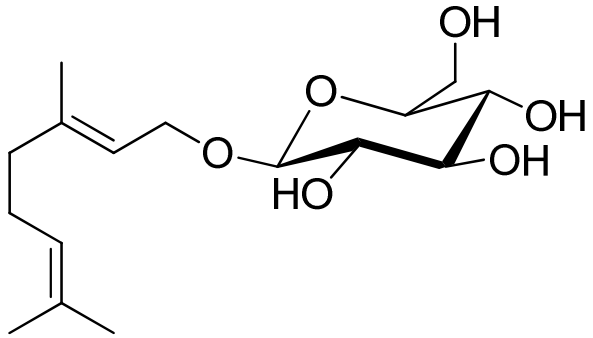
Brief history

2014 Founding initiative from Technical University Munich
2015 ACHEMA 1. Prize Industrial Biotechnology
2016 – 2017 EXIST Start-up Grant by
Federal Ministry for Economic Affairs and Energy
2017 Foundation of 4GENE GmbH
2018 Investment by HTGF, MBG, GOLDMANN
2021 Second Investment

The 4GENE Biotechnology Platform for Glucosylation comprises

- **Large enzyme library** of crop plant, bacteria and yeast **UDP-dependent glycosyltransferases**
- Known substrate specificities, Expertise in optimal screening approaches
- Broad spectrum of possible **substrates: alcohols, phenols, amines, thiols**
- **Products are O-, N- and S-glucosides**
- Stereospecific reactions producing ß-D-glucosides

- **Fast upscaling** of biotransformations **from g to kg amounts**
- Establishment of production processes
- Use of GRAS organism for biotransformation
- Sustainable processes
- **IP development** for production processes **with customers**



4GENE broad spectrum of substrates

Chemical type	Concrete examples	Chemical type	Concrete examples
Acyclic Monoterpene	Geraniol, Linalool, etc.	**Anthraquinone**	Alizarin
Monocyclic Monoterpene	Menthol, Perillyl alcohol, etc.	**Benzodioxole**	Sesamol
Bicyclic Monoterpene	Borneol, Myrtenol, etc.	**Fatty alcohol**	3-cis-Hexenol, 1-Octen-3-ol, etc.
Sesquiterpene	Farnesol, α-Bisabolol	**Hydroxy fatty acid**	16-OH-Palmitic acid 18-OH-Oleic acid
Phenolic	Eugenol, Guaiacol Tyrosol, etc.	**Furanone**	Furaneol, Sotolon, etc.
Flavonoid	Kaempferol, Quercetin	**Pyrone**	Maltol, Ethylmaltol
Coumarine	7-Hydroxycoumarin, Scopoletin	**Aminophenol**	Paracetamol
Quinoline	8-Hydroxyquinoline	**Thiophenol**	2-Methoxy-thiophenol
Stilbenoid	Resveratrol	**Amine**	Arom. + alipath. amines

4GENE Pharma spin off

Supporting your Goals in
Pharmacokinetics, Galenics, IP, and Patient Benefit

4GENE solutions for medicine

Pharmacological problems

Poor solubility

Poor chemical stability

Poor delivery

Bad absorption in the body

Rapid elimination

Unpleasant taste, esp. unacceptable for children and seniors

4GENE Technology Platform

4GENE's solution: bioactive glucosides

Water solubility increased 2 – 5000 fold

Chemical and physical stability increased

Better bioavailability

Therapeutic efficacy promoted ?

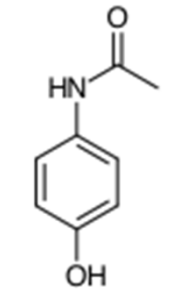
Pharmacokinetics improved ?

Prodrug, depot / retard function

Toxicity reduced ?

Taste and smell modified

Paracetamol



Paracetamol

Paracetamol is a Non-Opioid-Analgeticum and Antipyreticum.

On WHO Model List of Essential Medicines

Dose for adults 3-4 x 500 - 1000 mg (maximal 4000 mg / 24 hours).

Mode of action not finally elucidated. Inhibition of prostaglandin synthesis and endocannabinoids involved.

Overdose > 4000 mg / day: Liver toxicity !

Review > J Hepatol. 2017 Dec;67(6):1324-1331. doi: 10.1016/j.jhep.2017.07.005.
Epub 2017 Jul 20.

Acetaminophen (APAP) hepatotoxicity–Isn't it time for APAP to go away?

William M Lee [1]

Affiliations + expand

PMID: 28734939 PMCID: PMC5696016 DOI: 10.1016/j.jhep.2017.07.005

Free PMC article

Abstract

Acetaminophen (APAP) is the most commonly used drug for the treatment of pain and fever around the world. At the same time, APAP can cause dose-related hepatocellular necrosis, responsible for nearly 500 deaths annually in the United States (US) alone, as well as 100,000 calls to US Poison Control Centers, 50,000 emergency room visits and 10,000 hospitalisations per year. As an over-the-counter and prescription product (with opioids), APAP toxicity dwarfs all other prescription drugs as a cause of acute liver failure in the US and Europe, but it is not regulated in any significant way. In this review the ongoing controversy surrounding the proper role for this ubiquitous pain reliever: its history, pathogenesis, clinical challenges in recognition and management, and current regulatory status are highlighted. A new solution to a 50-year-old problem is proposed.

Keywords: APAP; Acetaminophen; Hepatotoxicity.

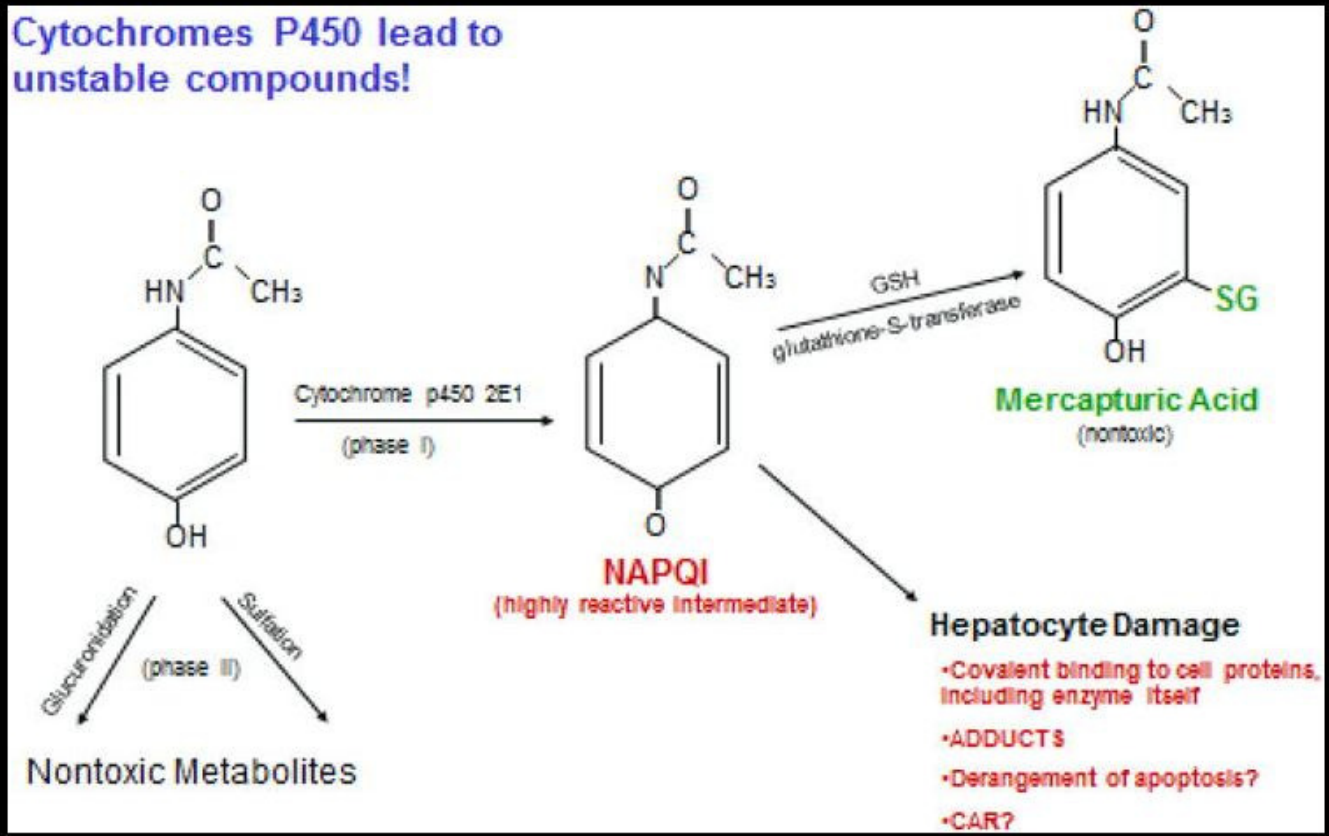
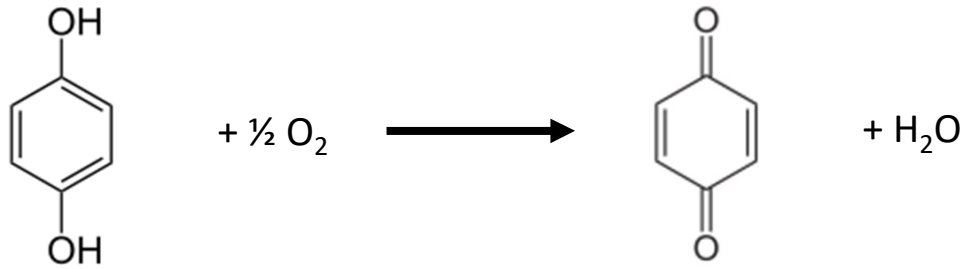


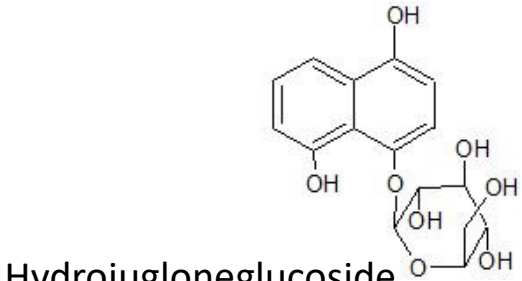
Figure 2 Biochemical pathways of acetaminophen metabolism. Only small amounts of NAPQI are formed unless the capacity for glucuronidation and sulfation is exceeded. Even then, glutathione supplies sulfhydryl groups that detoxify NAPQI to mercapturic acid, which is excreted in the urine. When glutathione is exhausted, then NAPQI binds to cell proteins disrupting cell function, the full details of which remain poorly understood.

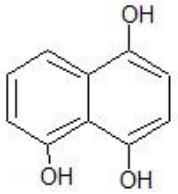
Hydroquinone-glucoside

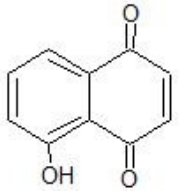
Hydroquinones easily oxidize to quinones



Substituents at Hydroxy-group can block this oxidation



Hydrojugloneglucoside + H_2O → Glucose + 

Hydrojuglone + ½ O_2 → 

Juglone

Paracetamol-ß-D-Glucoside

Paracetamol-ß-D-Glucoside synthezised
Patent application for process filed by 4GENE

Expected advantages:

Retard-effect

Lower toxicity

Larger therapeutic range

Short Profile and Contact

4GENE GmbH is a startup from Technical University Munich. Based on long-term research and focused R&D in a pre-founding phase, expertise and IP for flavor glucosides
as releasable storage forms of flavorings and aromas was gathered. Founding 4GENE in late 2017 led to B2B commercialization of pleasant bound flavorings and aromas as
FLAVOR-ON-DEMAND and of releasable warning odors as SNIFF&SAVE®. Some 50 bound flavors, aromas, and odors build the portfolio of 4GENE.
Recently, with 4YOURMASK® there is also a solution offered B2C. 4GENE is currently extending its activities to pharmaceuticals.

4GENE's glycosylation biotech platform is the base for functionalization of pharmaceutical compounds and is **offered as a B2B service** for customer's target compounds.

Contact:
thilo.fischer@4gene.de, fc.huang@4gene.de
https://www.4gene.de/

Lise-Meitner-Str. 30, D 85354 Freising, Germany, mobile: +49 (0)157 8641 5814, phone: +49 8161 1850900