DISCOVERING BIOACTIVE SUBSTANCES IN THE FOOD CHAIN

Dr. Joseph Schwager
DSM Nutritional Products
Basel, Switzerland

Joseph.Schwager@dsm.com

Elements of the presentation

- Bioactives and their importance in nutrition
- Concepts of screening and its application in nutrition science
- Identifying bioactives present in the food chain
- From identification to application in the real world

Nutrition and health

- (Pharmaceutical approach to bioactives)
- Food components condition and impair/improve our health
- Ethnobotanical evidence
  - Accumulation of empirical knowledge at the food/health interface
  - Different patterns of nutrition in different societies
  - Association of types of nutrition and benefits on health conditions
- ‚Du bist, was du isst' – (‚you are what you eat')
- Rise (and fall) of functional food / nutraceuticals

Identification of bioactives in the food chain

<u>The screening cascade</u>

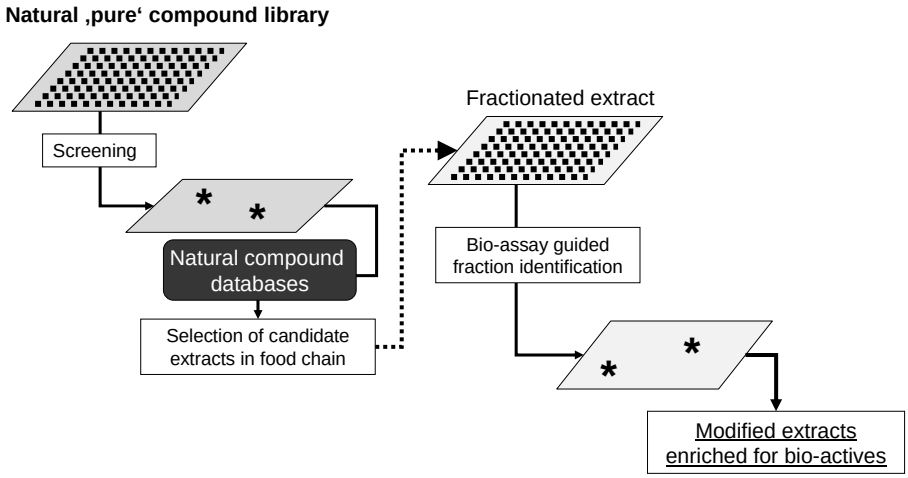
- Selection of health indication
- Definition of target (moelcular, cellular)
- From primary screening assays to lead compounds
- Efficacy and safety
- Steps from bench to product: molecular target → humans

Health indications and screening approach

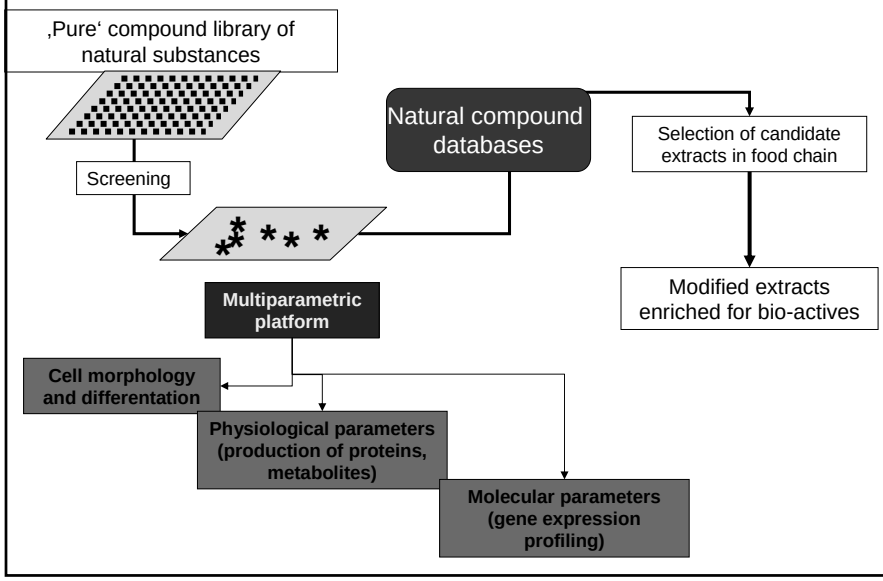
Definition and selection of molecular target

- Indication *Diabetes*: Receptor, ligand to receptor
- Indication *Joint Health - Arthritis*: enzymes
- Indication *Neurodegenerative diseases – mood/mental performance*: re-uptake of neurotransmittors

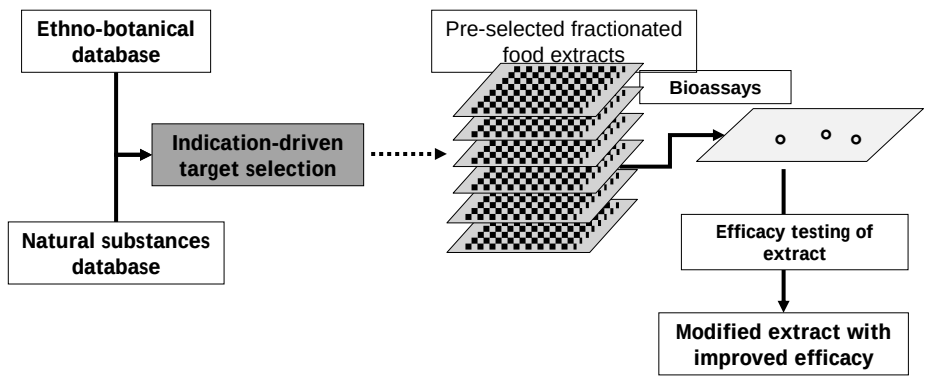
Directional positive nutritional screening



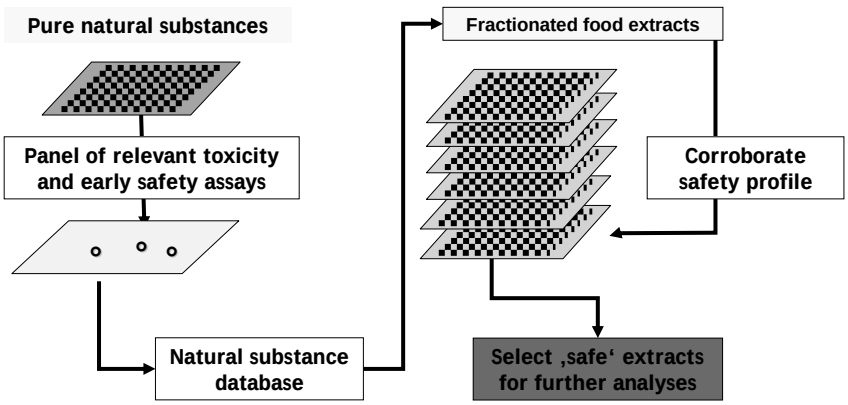
Complex (high contents) screening



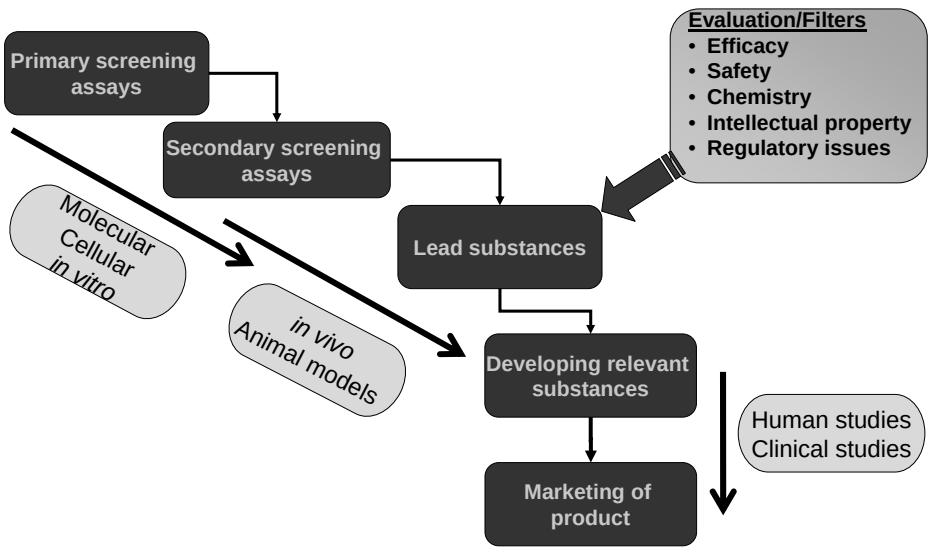
Reverse nutritional screening



Negative nutritional screening

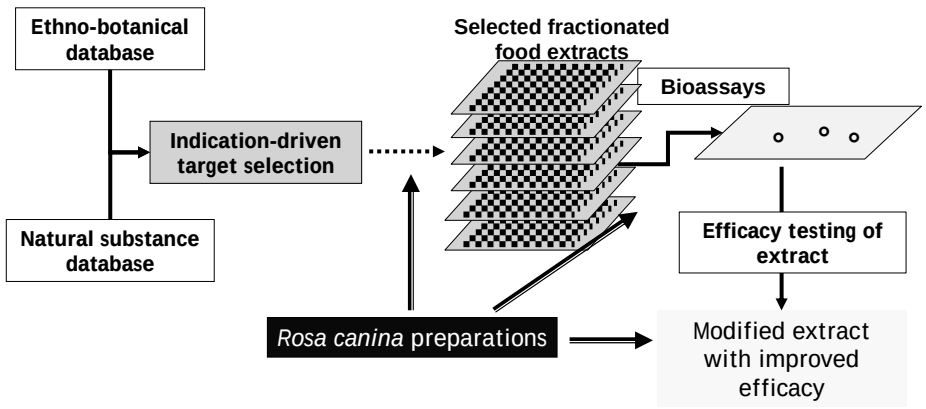


Screening cascade (in an environment of nutrition industry)



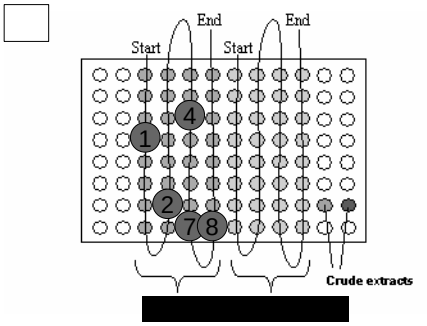
Example for Nutritional Screening: Rose hip (*Rosa canina*)

Rationale of *REVERSE SCREENING* (adapted from Schwager *et al*. Curr Op Biotech 2008)



Bio-assay guided fractionation

Testing fractions in bioassays (*i.e.* enzyme inhibition, receptor binding, production of proteins in cellular response to stimuli, metabolites)



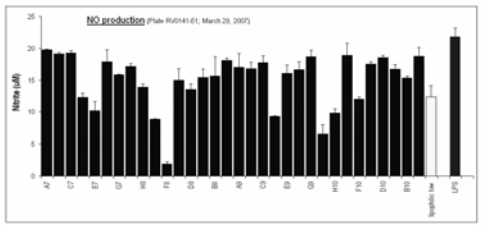
High degree of automatization/robotization

Adaptation to high throughput screening platforms

Bioactives identified in *Cajanus cajan (*pigeon pea*)*

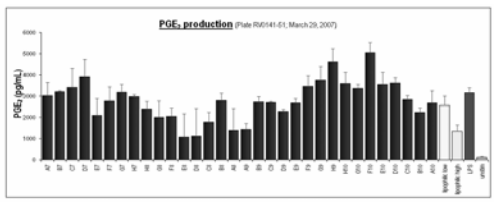
Rationale and approach

- Fractionation of *Cajanus cajan* extracts by standard procedures
- Individual testing of inhibitory potential of each fraction (in NO and PGE_2 production)
- Identifying of ‚hot spots'
- Structure elucidation of material contained in active wells

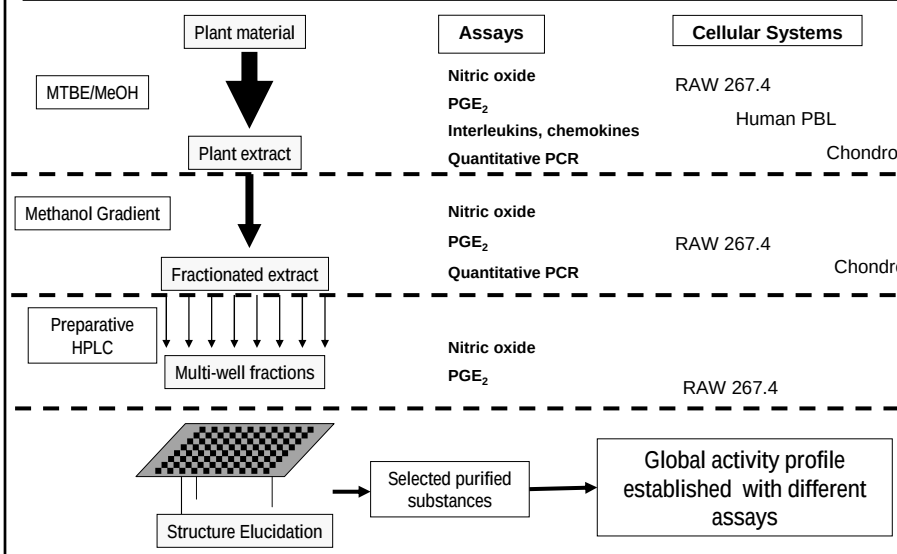


Outcome

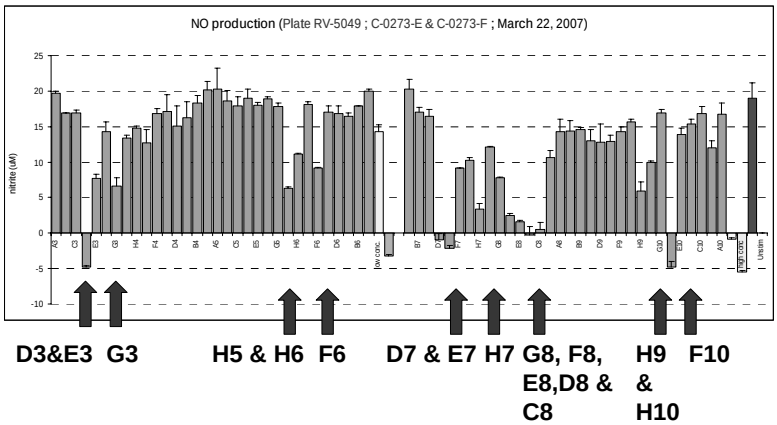
- Numerous ‚hot spots' in NO inhibition profile; this is consistent with the overall activity of the extract
- Some hot spots identified in the PGE_2 inhibitory profile
- The two profiles are not overlapping



Rationale of bio-assay guided fractionation



Anti-inflammatory effects of Rose hip constituents: Nitric oxide production



D3&E3 G3 H5 & H6 F6 D7 & E7 H7 G8, F8, E8,D8 & C8 H9 & H10 F10

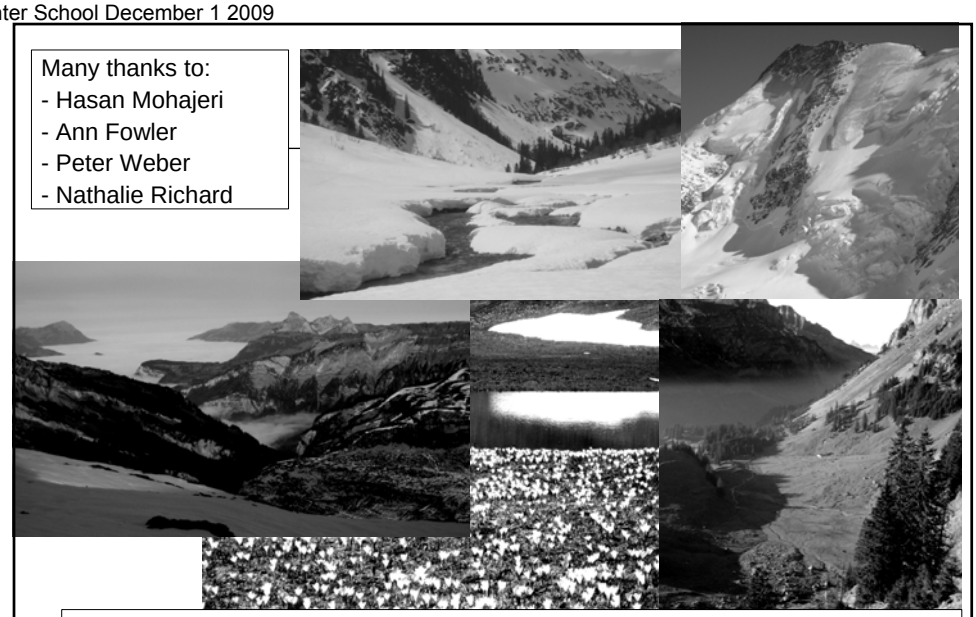
Rose hip extracts: fractionation /structure identification

Table 3: Target and Isolated Peaks:

Peak-No.	RT (min) [1]	Megdex	contained in fraction	MW [2]	Structure
1	28,01	2706	C-0273-S-01 ?	0	- [3]
2	30,40	2945	C-0273-S-02	278	Linolenic acid
3	31,37	3036	C-0273-S-03, -04	280	Linoleic acid
4	31,83	3078	C-0273-S-05	456	I (Terpenoid)
5	32,06	3099	C-0273-S-06, -07, -08	256	Palmitic acid
6	33,18	3202	C-0273-T-06, -07, -08	936	II (Glycolipid)
7	33,74	3245	C-0273-U-04, -05	774	III (Glycolipid)
		3340	C-0273-U-06	914	IV (Glycolipid)
8	37,70	3614	C-0273-U-06	0	- [3]
9	38,55	3692	C-0273-U-10	0	- [3]

[1]

Many thanks to:
- Hasan Mohajeri
- Ann Fowler
- Peter Weber
- Nathalie Richard



Additional reading:

- **Current Opinion in Biotechnology Volume 19, issue 2 /April 2008**
- **Schwager J, Fowler A & Weber P. Challenges in discovering bioactives for the food industry. *Current Opinion in Biotechnology* 2008, 19:66-72**

Questions (*ex officio*)

- What is the state of the art within the field in question?
- What are the hypotheses?
- Which results have been achieved?
- What does future work focus on?

Questions (*ex officio*) /Answers (*quoque ex officio*)

- What is the state of the art within the field in question?
  - **High level of tools in analytical and preparative platforms in natural product chemistry, large databases**
  - **For pharmaceutical approaches: mature**
  - **For nutraceutical approaches: expanding**
- What are the hypotheses?
  - **Not unlimited universe of the bioactives. Redundances (dependent on indications)**
  - **Bioactives contribute to therapeutic approaches; prevention of diseases**
- Which results have been achieved (by described screening approaches)?
  - **Limited additional results to what is already published → virtual screenings**
  - **Corroboration of previous observations and screening results**
- What does future work focus on?
  - **Interactions between bioactives**
  - **Marketing potential of bioactives (dietary supplements, food ingredients)**
  - **Revival of interest of pharmaceutical industry in bioactives?**