



**INTERPHARMA  
PRAHA, a.s.**

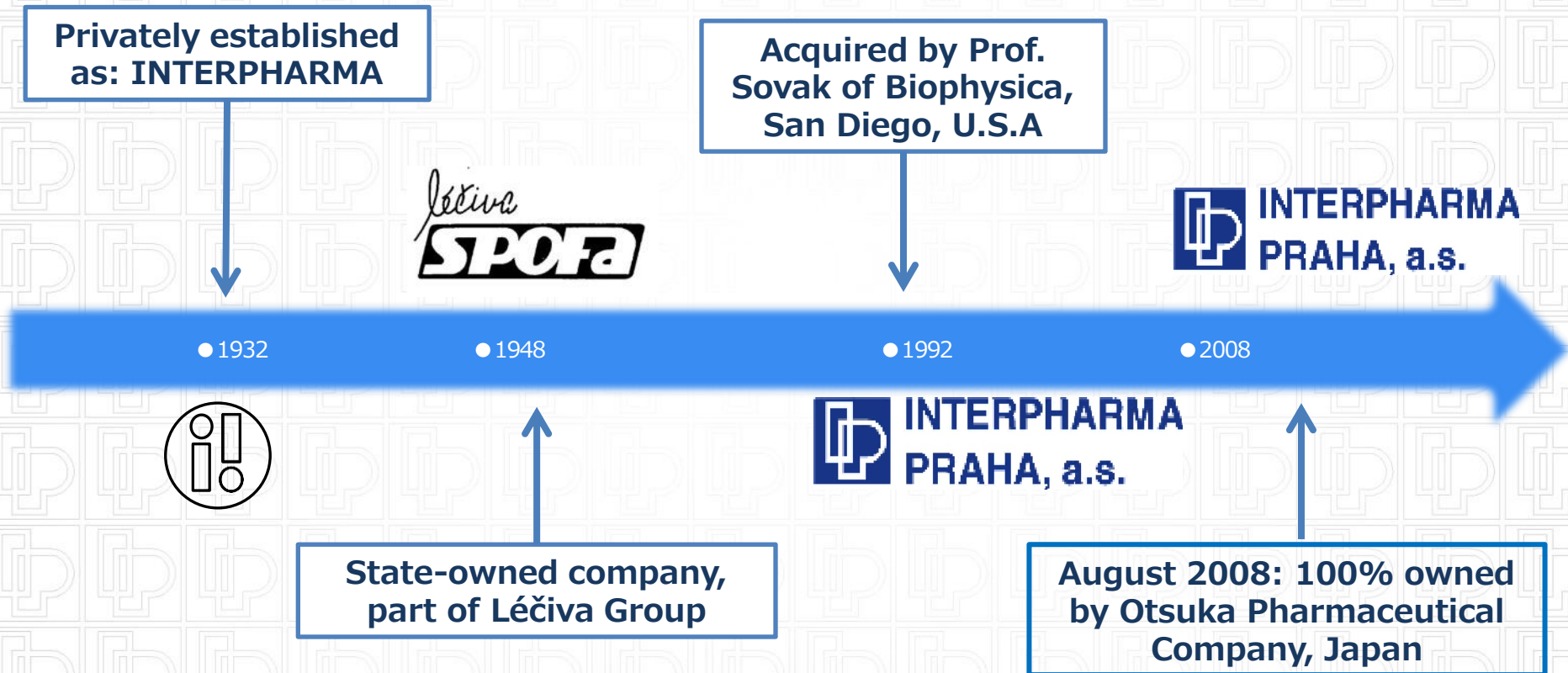
**GMP manufacturer of APIs, bulk  
Nutraceuticals and Cosmetics**

**20 let SVP výroby bulk doplňků  
stravy z rostlinných extraktů**

**Prepared by: Jiri Prokop, Research Chemist,  
Manufacturing Process Development Department**



**Interpharma Praha, a.s., is a pharmaceutical company founded in 1932 in Prague, Czech Republic, operating under GMP.**



**In 2008, Interpharma Praha has become a member of the Otsuka group, a Japanese Global Pharmaceutical Company.**

**We manufacture APIs, advanced intermediates, bulk, plant extract-based nutraceuticals and final cosmetic products.**

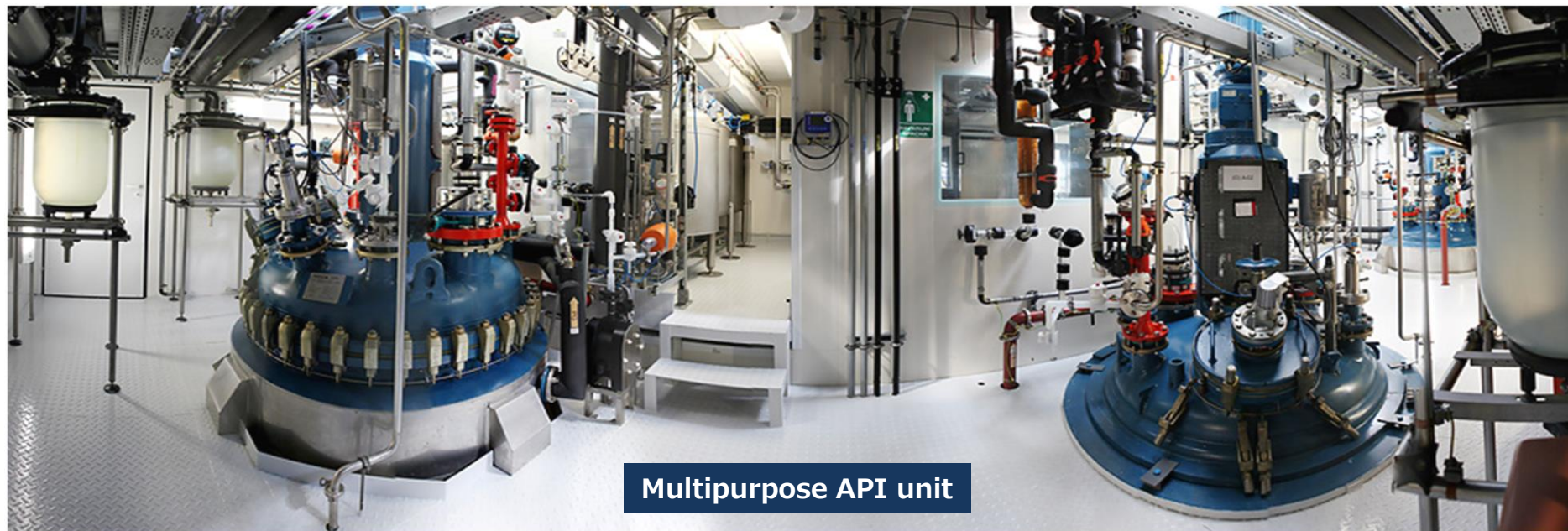
**For our Nutraceuticals, we focus on medicinal plant extracts with scientifically proven benefits. All our Nutraceuticals meet the same GMP production rules, quality controls and assurances, used in the manufacturing of APIs.**

**We have over 20 years of experience with sourcing plant extracts from China and India (Resveratrol, Boswellic acids, Curcumin, Baicalin, Silymarine).**

**From our well-known sources in Southern France, we have developed Regrapex-R - whole red grape extract enriched with pharmaceutically relevant quantities of Resveratrol.**



# Examples of Interpharma Praha production facilities



Multipurpose API unit



1Kilo Plant



1Kilo Plant- Clean Zone



Hydrogenation Unit



# Quality Control Laboratories: Instrumental Lab

QC – Instrumental lab



HPLC Equipment



GC-Headspace Equipment





# Microbiological Lab and Warehouse

Microbiological lab



Warehouse – Finished products



## Extra added values of IPP Nutraceuticals

- **IPP bulk Nutraceuticals - same GMP rules as for APIs. Approved in CR / EU as food supplements.**
- **Contain the highest possible amount of active ingredients, a result of thorough suppliers screening and using special IPP purification technologies.**
- **HPLC assay, using external standards, is used for testing the content of active ingredients in all raw materials.**
- **Strict control of raw materials from China / India, many years of experience led to choosing the most reliable suppliers.**
- **We test raw material for heavy metals by ICP-MS / AMA-AAS, residual solvents by GC headspace. Suppliers selected also by external analyses of pesticides, aflatoxines, organochlorinated compounds / PCB or PAH.**



# **Resveratrol and Red Wine Polyphenols** **worked-up to high-quality Nutraceuticals**

To offer our customers the benefit of a combination of high content natural Resveratrol and red grape polyphenols, we are manufacturing products containing natural *trans*-Resveratrol / *trans*-Resveratrol glucoside complex, manufactured under GMP (Good Manufacturing Practice):

**Regrapex-R® (min. 10% *trans*-resveratrol complex)**

**Regrapex-R® forte (min. 35% *trans*-resveratrol complex)**

**Resveratrol Glycon HP (min. 98% *trans*-resveratrol glucoside)**

Interpharma Praha has over 22 years of experience with Nutraceuticals, containing Resveratrol from *Polygonum cuspidatum* roots.





# Resveratrol - some important clinical data (2013)

Participants (number)	Design, oral RES dose, time (randomized, double-blind, placebo-control, unless specified)	Outcome (ClinicalTrials.gov, „Resveratrol and Clinical Trials: The Crossroad from In Vitro Studies to Human Evidence“, Carneiro JT, 2013)
Diabetes type 2 males (19)	10 mg RES, 1 month	Decreased insulin resistance.
Metabolic syndrome (34)	Placebo uncontrolled, 100 mg RES, 3 mon	Blood vessel function improved (FMD increased from 4 to 9%).
Patients on statin, at high risk (75)	Triple-blind, 8 mg RES in 350 mg Grape Ex, 6 mon, double dose for next 6 m	Lowered atherosclerosis risk factor (LDLox lowered by 20%).
Diabetes type 2 (62)	Placebo uncontrolled, 250 mg RES, 3 m	Improved systolic and diastolic blood pressures, lowered total and LDL cholesterol .
Obese insulin resistant (10)	Placebo uncontrol., 1, 1.5 or 2 g RES, 1 m	Improved insulin sensitivity and postmeal plasma glucose. Not dose dependent.
Coronary artery disease, stable (40)	10 mg RES, 3 m	Lowered atherosclerosis risk factor (LDL cholesterol lowered by 8%. Improved blood vessel function (improved endothelial function by 50%).
Patients on statin, at high risk (75)	Triple-blind, 8 mg RES in 350 mg Grape Ex, 12 m	Decreased inflammation markers: hsCRP by 26%, TNF $\alpha$ 19.8%, and fibrinolytics markers: PAI-1 by 16.8%, IL-6 / IL-10 by 24%.
Stable angina pectoris (116)	Active-controlled, 20 mg RES or 20 mg RES +112 mg Ca fructoborate (CF), 2 m	Decreased inflammation marker hsCRP: RES group by 60%, RES+CF group by 70%
Coronary artery disease (75)	Triple-blind, 8 mg RES in 350 mg Grape Ex, 6 mon, double dose for next 6 m	Lowered atherosclerosis risk (increased adiponectin by 10%, decrease of PAI-1, decreased non-HDL cholesterol). Inflammation suppressed.
Healthy subjects (20)	40 mg RES in 200 mg Polygonum extract, 1.5 m	Decreased oxidative stress markers (ROS, p47 <sup>phox</sup> , NF- $\kappa$ B, IKK $\beta$ , JNK, PTP-1B and SOCS-3 in PBMCs - peripheral blood mononuclear cells) and inflammatory markers (hsCRP by 29%, TNF $\alpha$ by 33%).
Healthy subjects (10)	Unblinded, 100 mg RES + 75 mg Grape Ex, taken 10 min. before high fat and calorie meal, measured within 5 hrs after meal	Decreased plasma lipopolysaccharides and oxidative and inflammatory markers in PBMCs (p47 <sup>phox</sup> , SOCS-3, Nrf-2, TLR-2, IL-1 $\beta$ , CD-14, Keap-1, NQO-1, GST-P1). Best results seen 3-5 hr after meal.
Obese men, post-menopausal women (19)	Placebo uncontrolled, 30, 90, 270 mg RES weekly, measured 1 h after intake	FMD (flow mediated dilation) improved by 65% with 30 or 90 mg RES, by 88% with 270 mg RES.
Obese men (11)	150 mg RES daily, for 1 month	Induced modest but consistent metabolic changes that mimic caloric restriction. Reduced sleeping and resting metabolic rate, activated AMPK, increased SIRT1 and PGC-1 $\alpha$ in muscles.
Healthy adult smokers (50)	500 mg RES daily 1 month, wash-out 1 mon, again 500 mg RES daily 1 mon	Decreased inflammation marker and triglycerides significantly. Increased total antioxidant status.
Healthy subjects (50)	8 mg RES in 133 mg Grape Ex, 2 months	Antioxidant capacity of blood and skin antioxidant power increased significantly. Skin moisturization and elasticity improved, skin roughness and wrinkles depth diminished. Intensity of age spots decreased.

# Regrapex-R

**whole red grape extract with 10% resveratrol complex**

## „Healthy cardiovascular system“

- **Made from high quality grapes grown in Southern France**
- **Standardized to 10% *trans*-resveratrol complex, predominantly of resveratrol glucoside, its better bioavailable form**
- **Polyphenols standardized to min. 50% (Folin method, as GAE)**
- **Maintains a natural balance of all salutary polyphenols (OPCs, flavonoids, phenolic acids, resveratrol, anthocyanines)**
- **Studies indicate that daily consumption of grape polyphenols induces a cholesterol lowering effect, probable explanation of the “French Paradox”, a lower incidence of cardiovascular diseases in wine regions of France, despite a high fat diet**





# Regrapex-R Forte

**whole red grape extract with 35% resveratrol complex**

## „Healthy cardiovascular system“

- **Made from high quality grapes grown in Southern France**
- **Standardized to 35% trans-resveratrol complex**
- **Polyphenols standardized to min. 50% (Folin method, as GAE)**
- **Maintains a natural balance of all salutary polyphenols (OPCs, flavonoids, phenolic acids, resveratrol, anthocyanines)**
- **Any desired concentration of Resveratrol in Regrapex-R can be provided as a custom blend**



# Resveratrol Glycon HP

**98% resveratrol glucoside**

**„Antioxidant for Skin protection & Healthy cardiovascular system“**

- **Highly purified *trans*-resveratrol-3-O-glucoside**
- **Made from roots of Japanese Knotweed (*Polygonum cuspidatum*), used in traditional asian medicines as lipid-lowering and anti-inflammatory**
- **Standardized min. 98% *trans*-resveratrol glucoside (HPLC assay), associated compounds controlled by HPLC**
- **Contains no other residual solvent than ethanol (by GC headspace)**
- **As a glucoside, it has better oral bioavailability and better water solubility, can be easily formulated into functional drinks**





# Hepacept®

## standardized purified plant extract composition

### „Liver protection“

- Made from 6 concentrated, purified and standardized plant extracts, used in traditional asian medicines as anti-inflammatory and liver regeneration treatments.
- Contains: Japanese Knotweed (resveratrol), Frankincense (acetylboswellic acids), Turmeric (curcumin), Milk Thistle (silymarin), Scullcap (baicalin), with anti-inflammatory and liver protective effects. Small amount of Black Pepper extract (piperine) is added for increasing bioavailability.
- Proven synergistic effect of the components (on cell cultures) which are working better together than alone.



# Acetylboswellic acids (one of Hepacept components)

- extracted from *Boswellia serrata*

„Joint relief, anti-inflammatory“

- Made from resin of Olibanum tree (*Boswellia serrata*), an indian tree used in Ayurveda for anti-inflammatory treatment.
- Standardized to min. 30% of the most active boswellic acids ABA and AKBA.
- Content determined by HPLC assay as weight %, not just % by titration.
- Boswellic acids are used in joint relief food supplements against arthritis and chronic liver inflammations, asthma or skin afflictions.

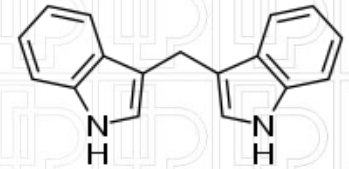
ABA = Acetyl- $\beta$ -boswellic acid, AKBA = Acetyl-11-keto- $\beta$ -boswellic acid





# Diindolylmethane (DIM)

DIM synthetic, 98%



## Diindolylmethane (DIM) as a food supplement

- Proven to maintain natural metabolism and balance of both female and male sexual hormones, proposed as a **breast or prostate cancer preventative**.
- **15 clinical studies** already completed in the U.S., Canada, UK or Germany, in patients with prostate / breast cancer or cervical dysplasia (as of 2021).
- **Interpharma Praha** has developed in 1999 a unique and efficient process for DIM, ordered by the U.S. company Bioresponse for their patented formulation.
- This **formulated DIM** was proven in clinical studies as far **more bioavailable** than regular crystalline DIM and is being sold as a food supplement in the U.S.
- In 2003, **IPP created DMF** for Bioresponse **enabling IND application**. Use of DIM is expected to increase as more evidence for its usefulness is emerging.
- **IPP** has been producing DIM using the same **GMP** rules as for the APIs since 2001, in a dedicated unit with MT amounts annually. We were **FDA inspected** for DIM as a dietary ingredient in 2019.



**Advanced topical hair care, free-sale cosmetic product**  
**Manufactured at Interpharma Praha from 2002.**  
**Sold in both EU and non-EU countries.**



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