Mechanism of System K11

&

An updated aetiology of androgenetic alopecia

Ingredients in systemK11

systemK11™

High-Strength Metabolites &
Enriched Botanical Extracts

Targeted Hair Nutraceutical

Dietary Supplement · 120 Tablets

Supplement Facts
Serving Size: 4 Tablets
Daily Servings Per Container: 30

	Amount Per Serving	% Daily Value
Calories	5	
Total carbohydrate	2g	<1%*
Dietary Fiber	2g	7%*
Vitamin C (as ascorbic acid)	24 mg	27%
Vitamin D (as cholecalciferol)	5 mcg	25%
Vitamin E (as *d*-alpha-tocopheryl succinate)	12 mg	80%
Thiamin (as thiamin mononitrate)	3 mg	250%
Riboflavin	4 mg	308%
Niacin	9 mg	56%
Vitamin B_{12} (as cyanocobalamin)	8 mcg	333%
Iron (as ferrous fumarate)	14 mg	78%
Iodine (from kelp)	88 mcg	59%
Magnesium (as magnesium oxide & magnesium bisglycinate chelate)	350 mg	83%
Zinc (as zinc sulfate)	20 mg	182%
Chromium (as chromium picolinate)	40 mcg	114%
Sodium	5mg	<1%
systemK11™ Proprietary Formula	**1560mg**	†
Fenugreek seed fiber extract (FenuLife® EXTRA), Broccoli seed concentrate (10% sulforaphane glucosinolates with myrosinase) (Activated BroccoRaphanin®), Pine bark extract (85% proanthocyanidins), Fenugreek seed extract, Dihydroberberine (GlucoVantage®), Soybean extract (40% isoflavones), L-Ergothioneine (MitoPrime®), Black pepper fruit extract (BioPerine®)		
N-Acetyl cysteine	60 mg	†
L-Methionine	30 mg	†
PABA (Para-aminobenzoic acid)	20 mg	†
Silicon (from silicon dioxide)	20 mg	†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily value not established.

Other ingredients: microcrystalline cellulose, stearic acid, dicalcium phosphate, croscarmellose sodium, coating (hypromellose, macrogol, hydroxypropyl cellulose) and magnesium stearate. **Allergen warning: contains soy.**

INSPIRED BY INNOVATIONS IN GENE EXPRESSION ANALYSIS, SYSTEMK11 WAS EXECUTED IN THE NEW PARADIGM OF HAIR LOSS SCIENCE*

Instructions: Take 4 tablets per day with meals, or up to 30 minutes before eating.

Do not use if pregnant, breastfeeding, using medication for diabetes or macrolide antibiotics. If taking other medication or have any medical condition consult a doctor before taking. Do not use if safety seal is damaged or missing.

Formulated in London, UK · Blended in USA for:

Systems Trichology NJ, LLC. Five Greentree Centre, 525 Route 73 North Ste 104, Marlton, NJ, 08053
contact@k11.co, +1 (917) 893 4422.

Vegan · Patent Pending · www.K11.co

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*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Warning: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep out of reach of children. In case of accidental overdose call a doctor or poison control center immediately.

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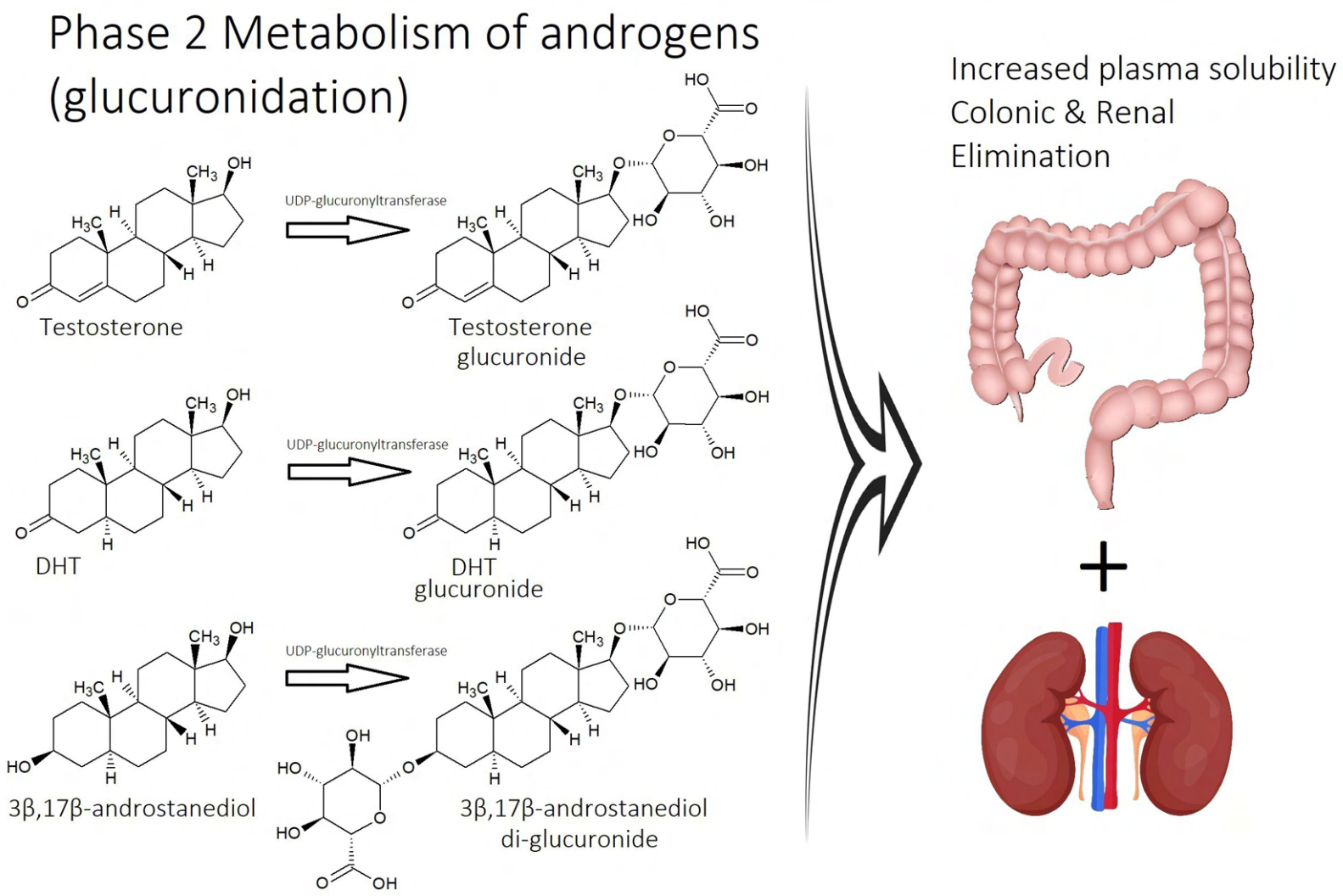
Notes
- Procyanidin B2 and B3 is in pine bark extract
- Gallactomannan is a fenugreek seed fiber extract

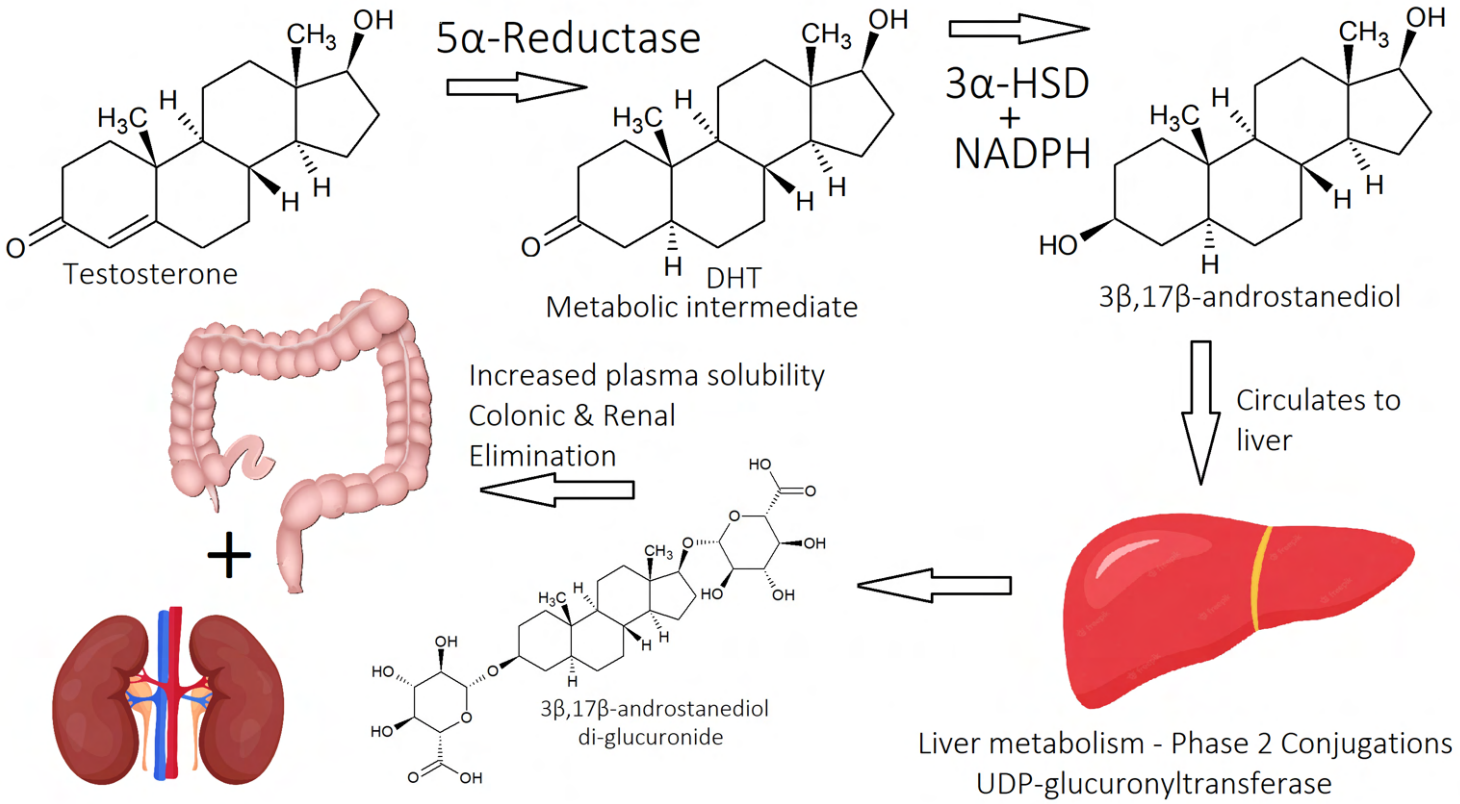
Section A:

Biochemistry of normal hair

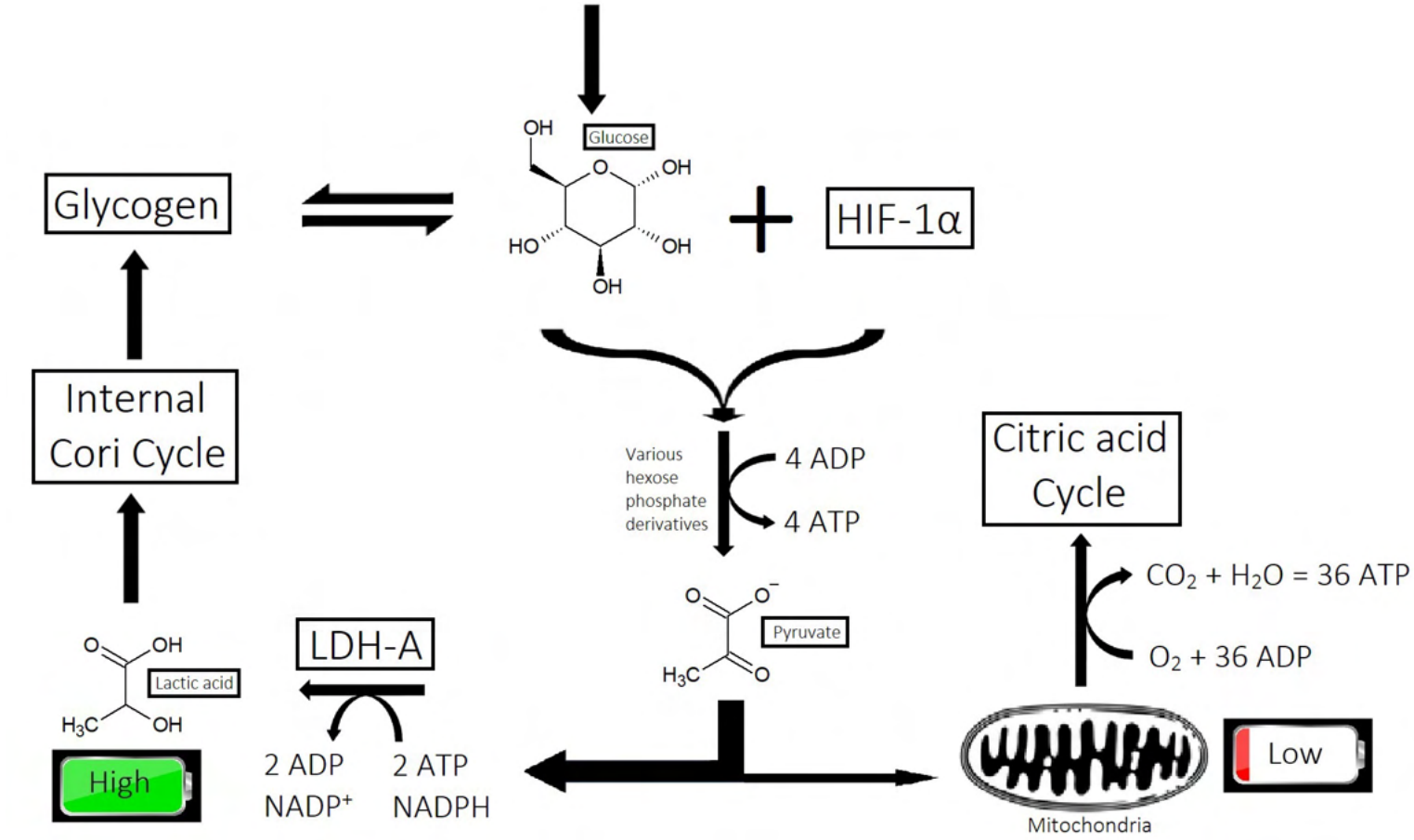
- Androgens are modulated to an extent in the skin
- However, most of the metabolism of androgens occurs in the liver
- Androgens have polar groups, such as sulphates or glucuronic acid (in image) attached
- The more polar androgen conjugate is circulated to the kidneys or the colon for elimination from the body



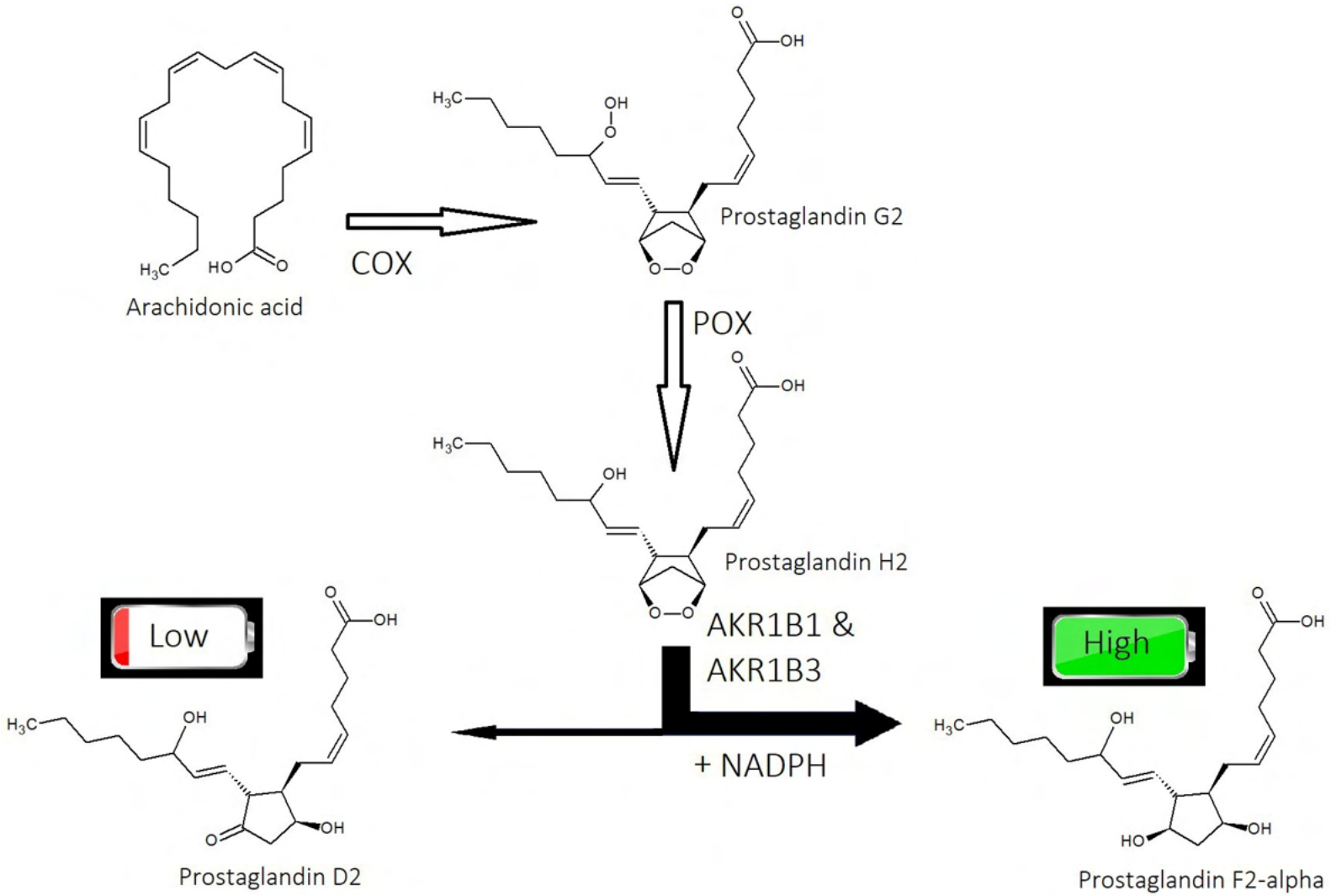
- DHT is also metabolised for elimination in the scalp
- DHT represents an intermediate in the elimination of testosterone
- The enzyme that degrades DHT is called 3α-hydroxysteroid dehydrogenase (3α-HSD)



- The hair follicle follows an energy metabolism unlike other tissues of the body
- A factor called HIF-1α is expressed to sustain anerobic glycolysis of glucose into lactate
- The reaction is irreversible, to protect mitochondria from burnout
- The hair follicle has an ‘internal’ Cori cycle to store the lactate as glycogen to feed the hair follicle during anagen growth



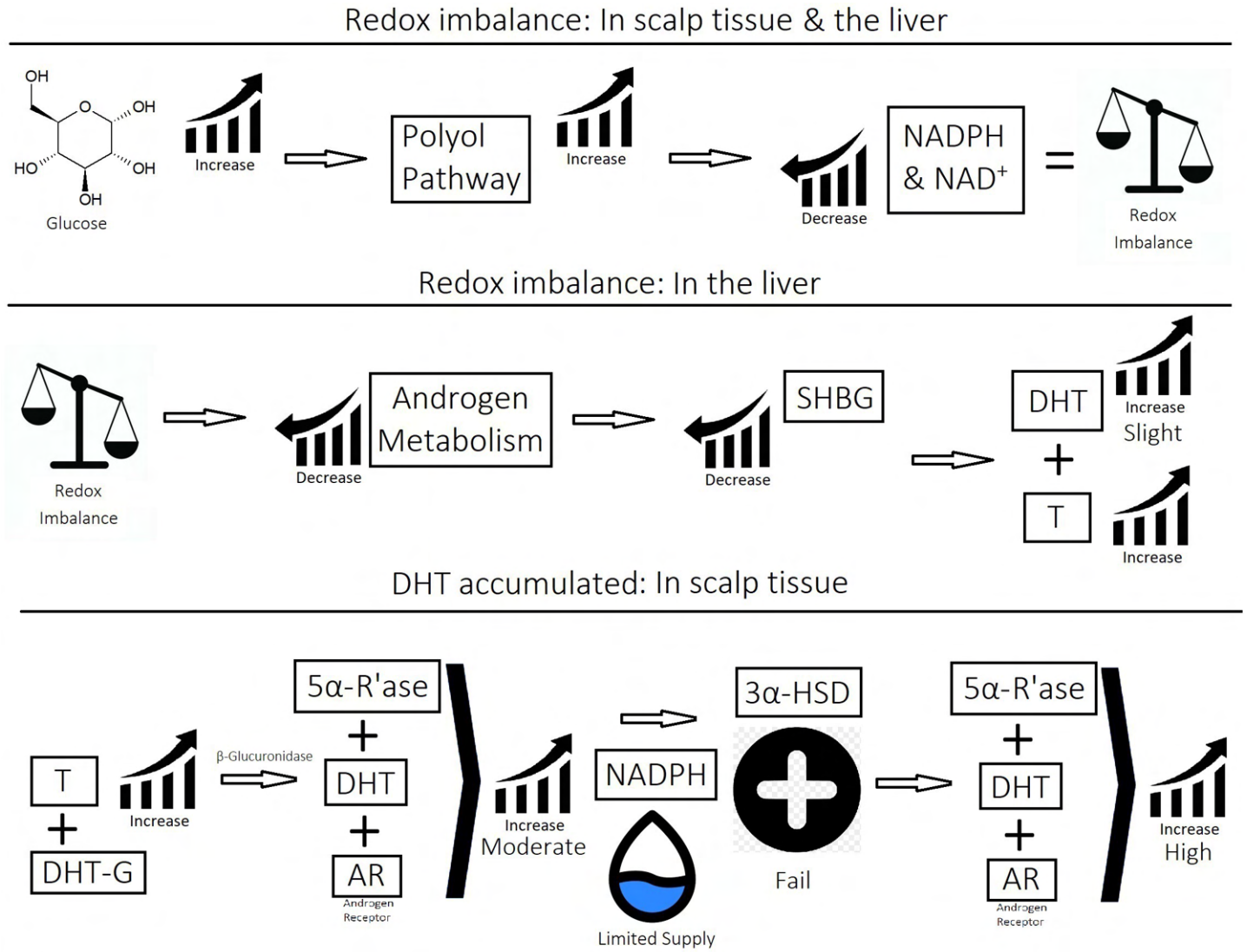
- The scalp is also a site of active prostaglandin synthesis
- The prostaglandins modulate growth and fatty acid synthesis
- Prostaglandin F2-alpha dominates in healthy hair, requiring a reducing substrate for its synthesis
- The reducing substrate is NADPH



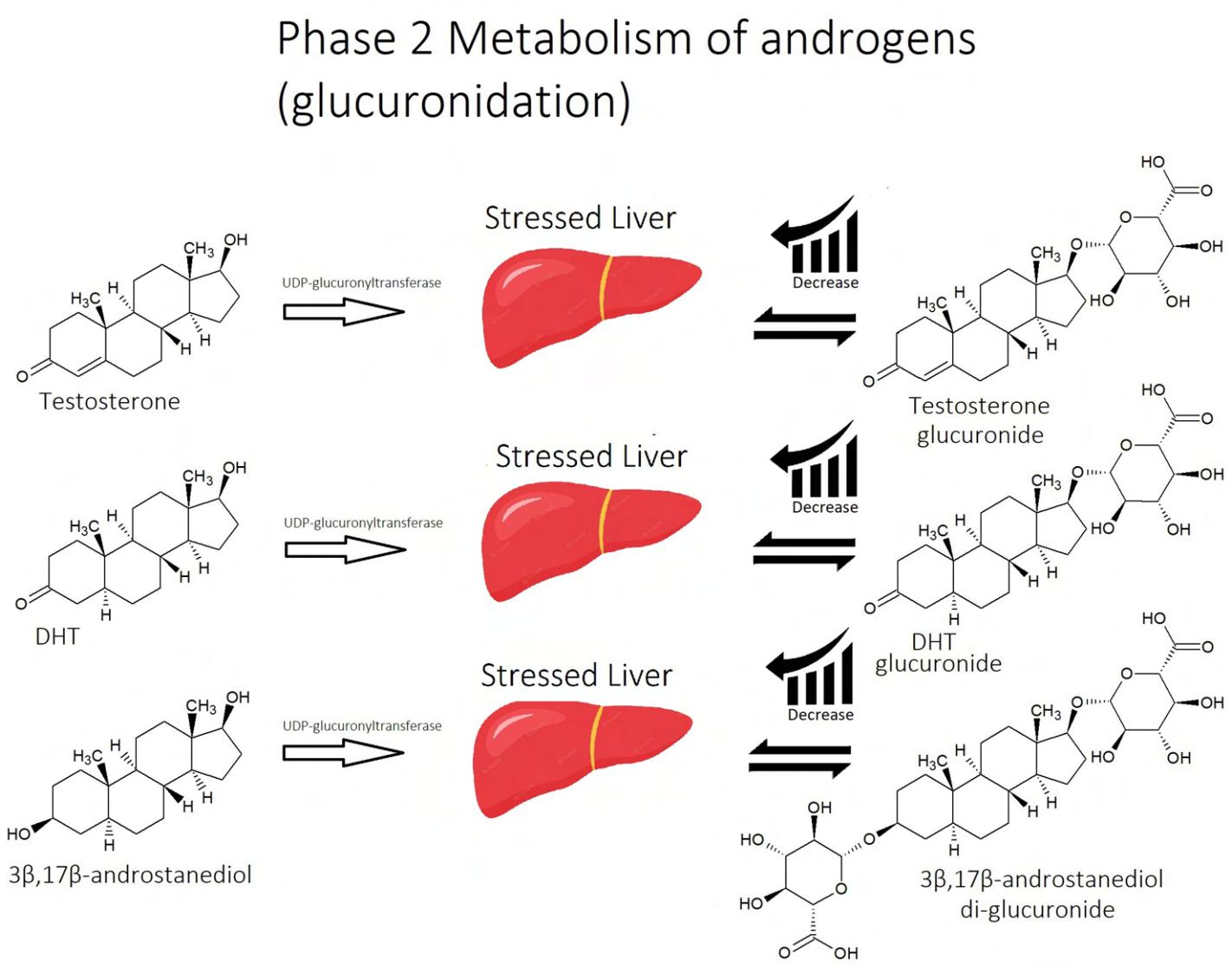
Section B:

Aetiology of androgenetic alopecia

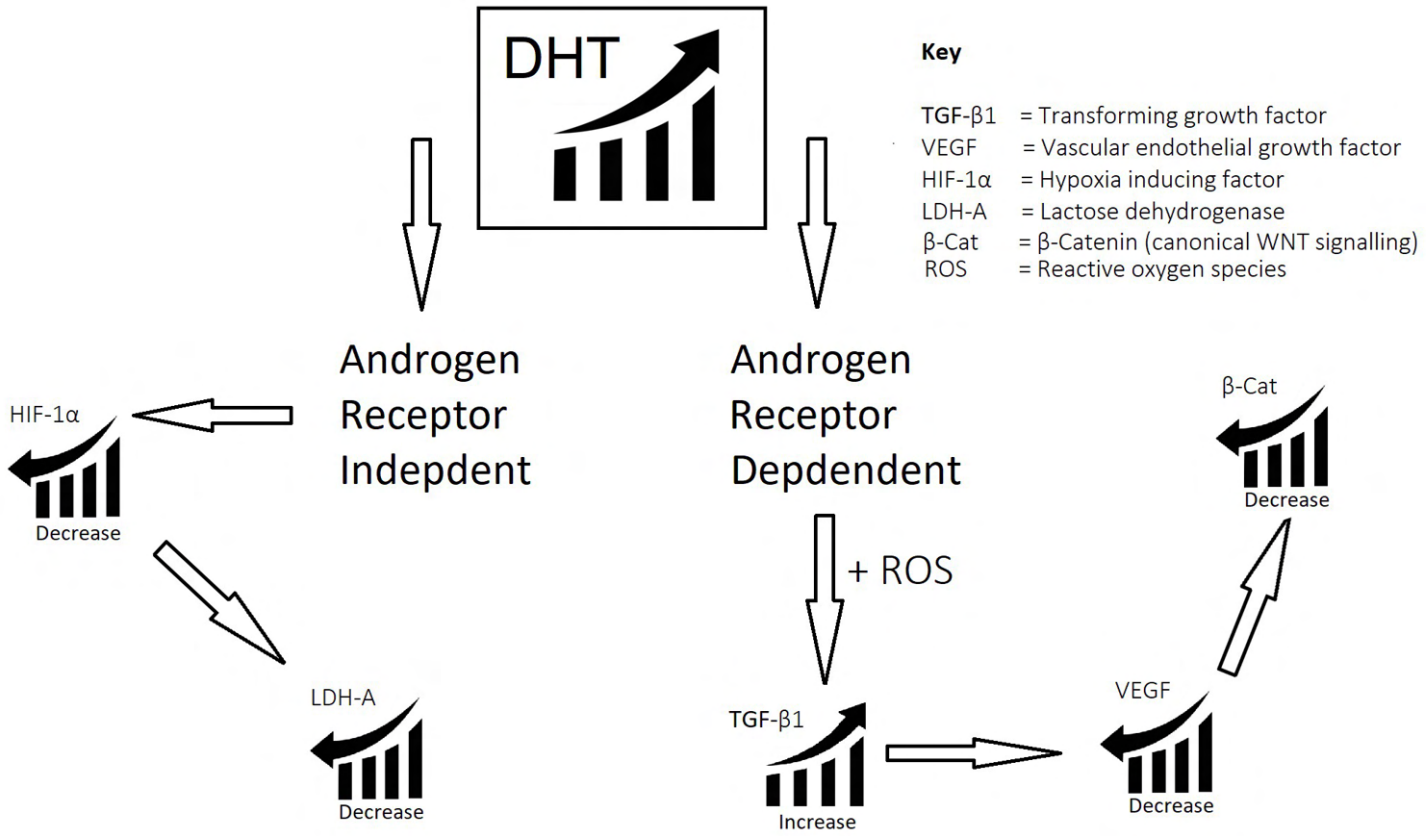
- An androgen abnormality causes systemic disruption
- The destructive power from dysregulated DHT is potentiated by a disruption to glucose metabolism
- High glucose starts the polyol pathway (converting glucose to fructose)
- The polyol pathway interferes with reducing substrates required for homeostasis (NADPH & NAD^+)
- High glucose also interferes with liver function, reducing its ability to conjugate DHT for elimination
- Lower levels are produced of a protein called SHBG that binds to and inactivates DHT
- Slightly higher T circulating to the scalp increases expression of 5α-reductase
- Due to low NADPH, 3α-HSD malfunctions
- DHT accumulates, the scalp starts to become mildly inflamed
- Inflamed scalp expresses β-glucuronidase, which returns circulating DHT-glucuronide to its free form
- DHT accumulates further



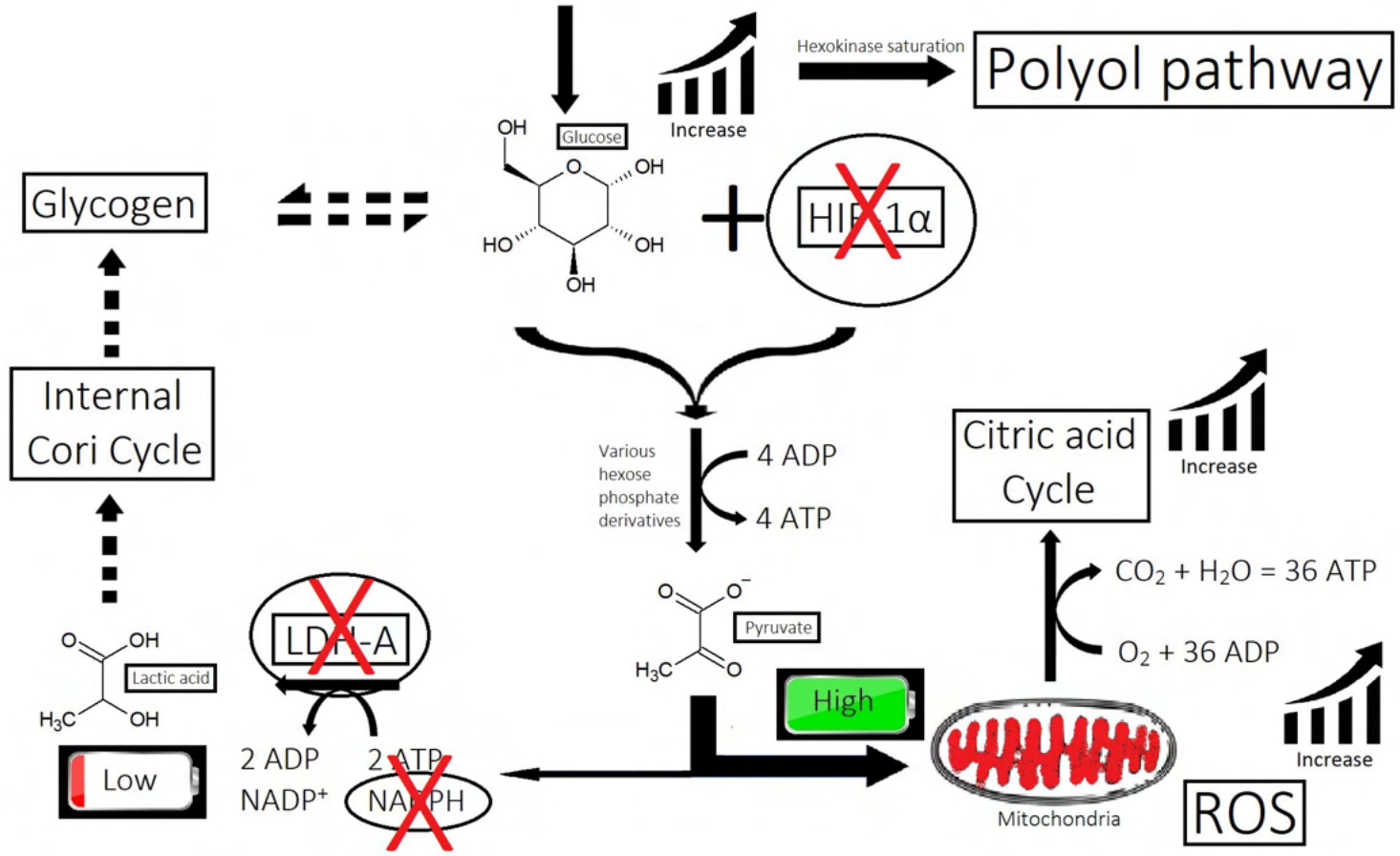
- As previously mentioned, stressed liver does not sufficiently metabolise DHT for elimination
- Although DHT-glucuronides are produced at a slower rate, there is enough to react with β-glucuronidases to produce free DHT
- When the scalp becomes inflamed, β-glucuronidase is expressed locally, capturing systemic DHT-glucuronides before they are eliminated



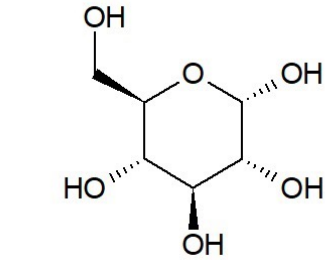
- Elevated DHT in scalp binds to the androgen receptor, increases the expression of TGF-β1 when reactive oxygen species are present
- TGF-β1 interferes with the canonical WNT signalling pathway
- DHT also reduces HIF-1α independently of the androgen receptor
- This reduces the amount of lactose dehydrogenase (LDH-A)
- Consequently glucose metabolism is interfered with
- Reduced HIF-1α also interferes with angiogenesis, causing reduced blood flow



- The degradation of HIF-1α means that the normal route of glucose to lactate is antagonized, which attenuates the Cori cycle, reducing the amount of glycogen available to hair follicles during growth
- Glucose metabolism becomes predominantly aerobic, creating anoxia, stressing mitochondria, and generating a high output of reactive oxygen species



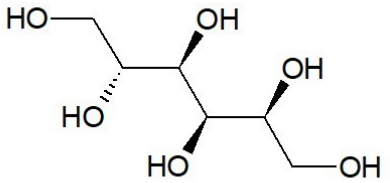
- In parallel with a high rate of aerobic respiration, the polyol pathway becomes more active
- This mainly occurs in hyperglycaemic events (with high sugar eating)
- The polyol pathway reduces the amount of NADPH and NAD^+
- This interferes with the metabolism of DHT and the synthesis of prostaglandins



Glucose

NADPH

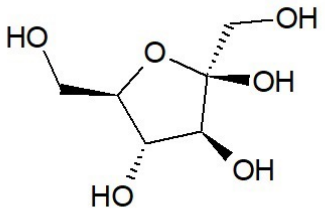
$NADP^+$



Sorbitol

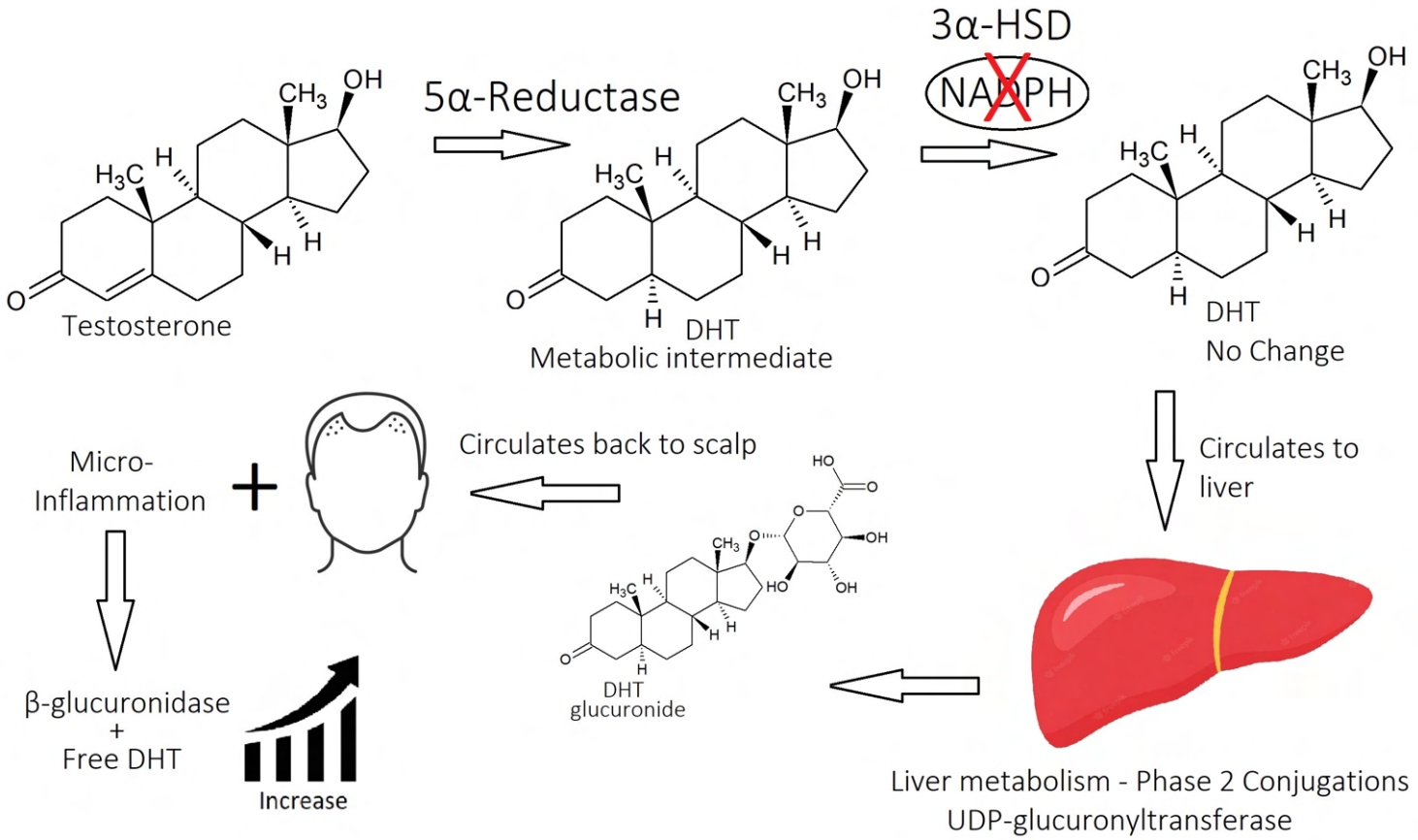
NAD^+

NADH

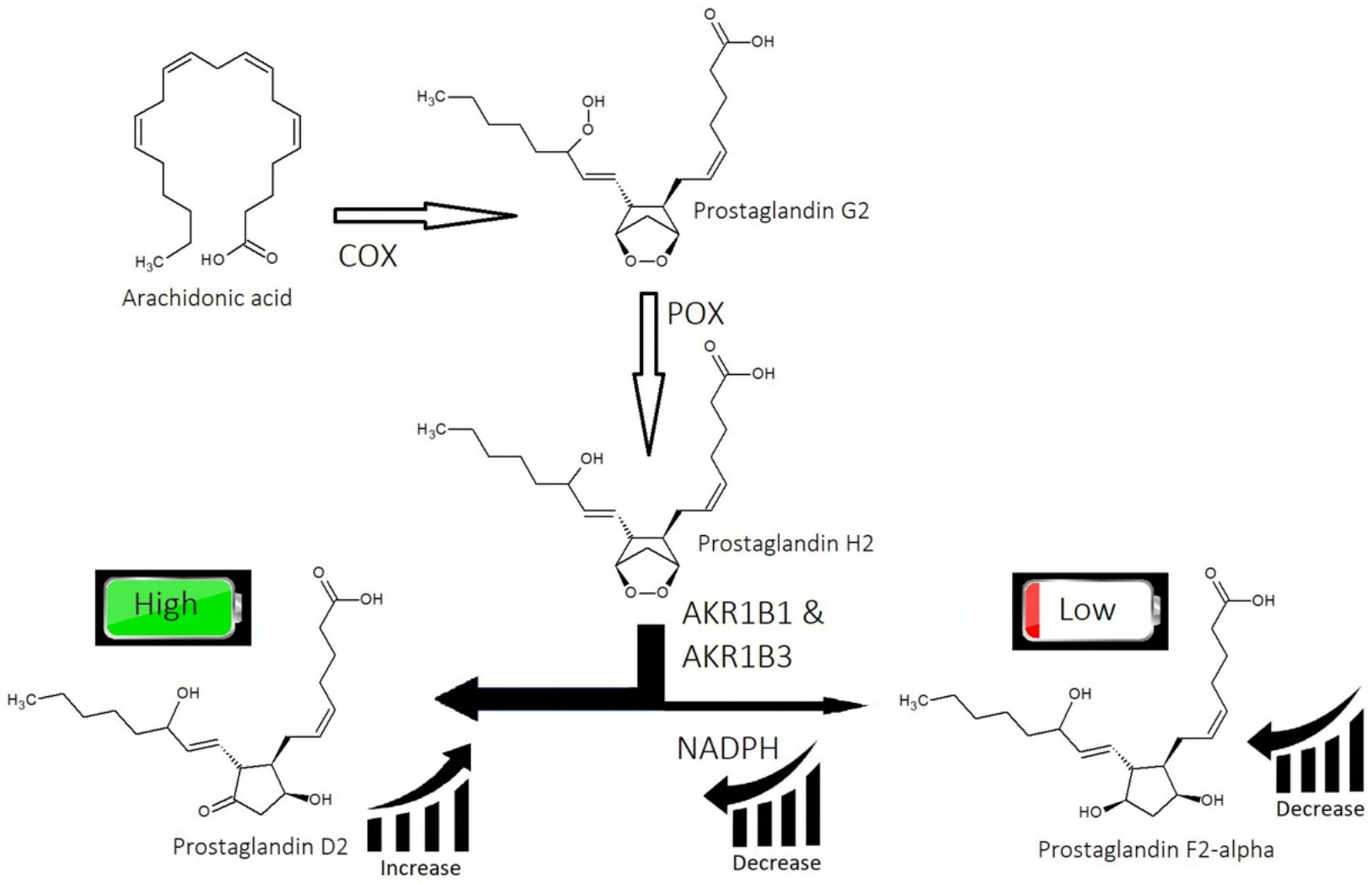


Fructose

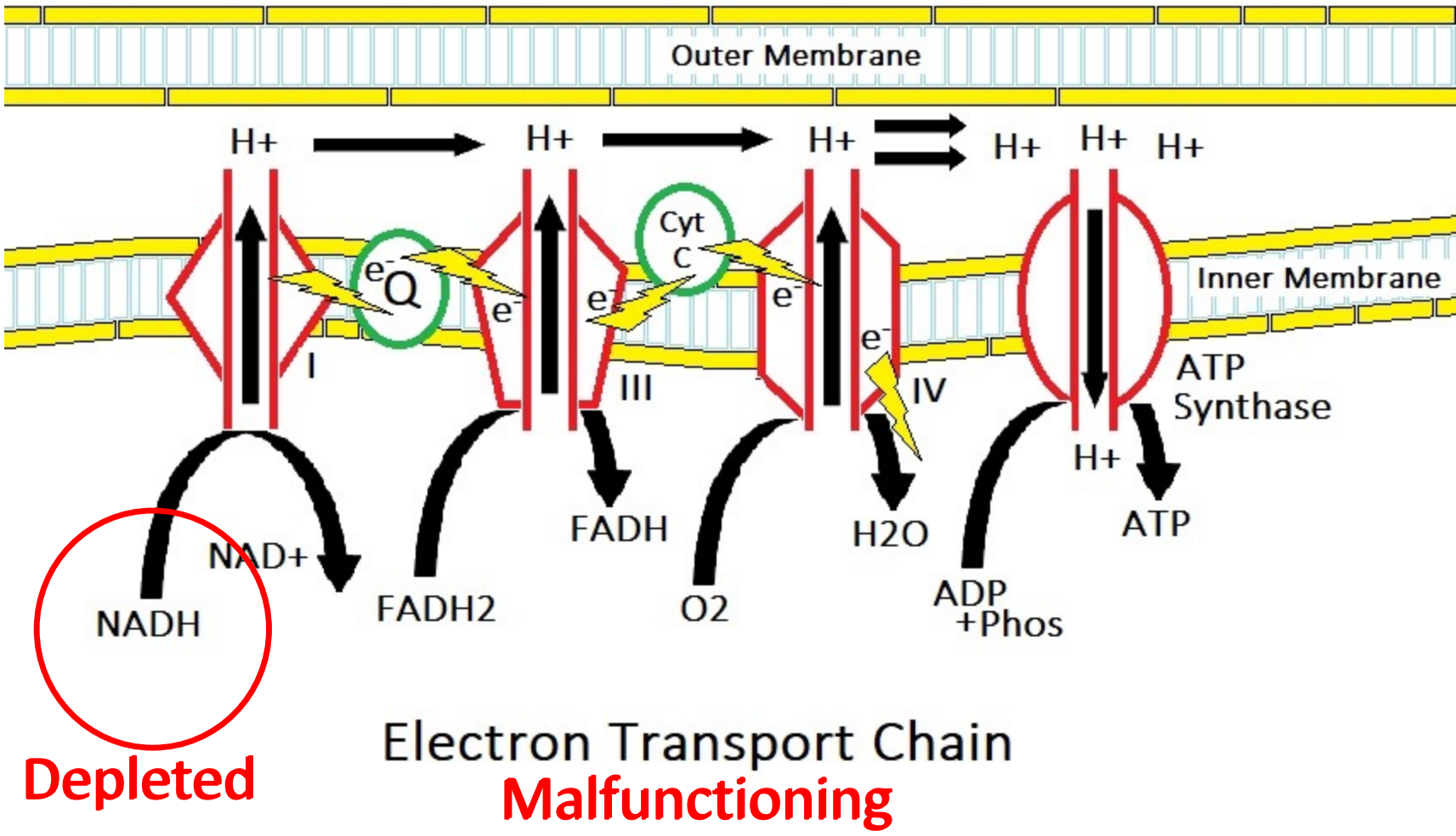
- With low availability of NADPH the enzyme 3α-HSD malfunctions, causing DHT to accumulate
- The consequent inflammation increases expression of β-glucuronidase, which, as previously mentioned, increases DHT further



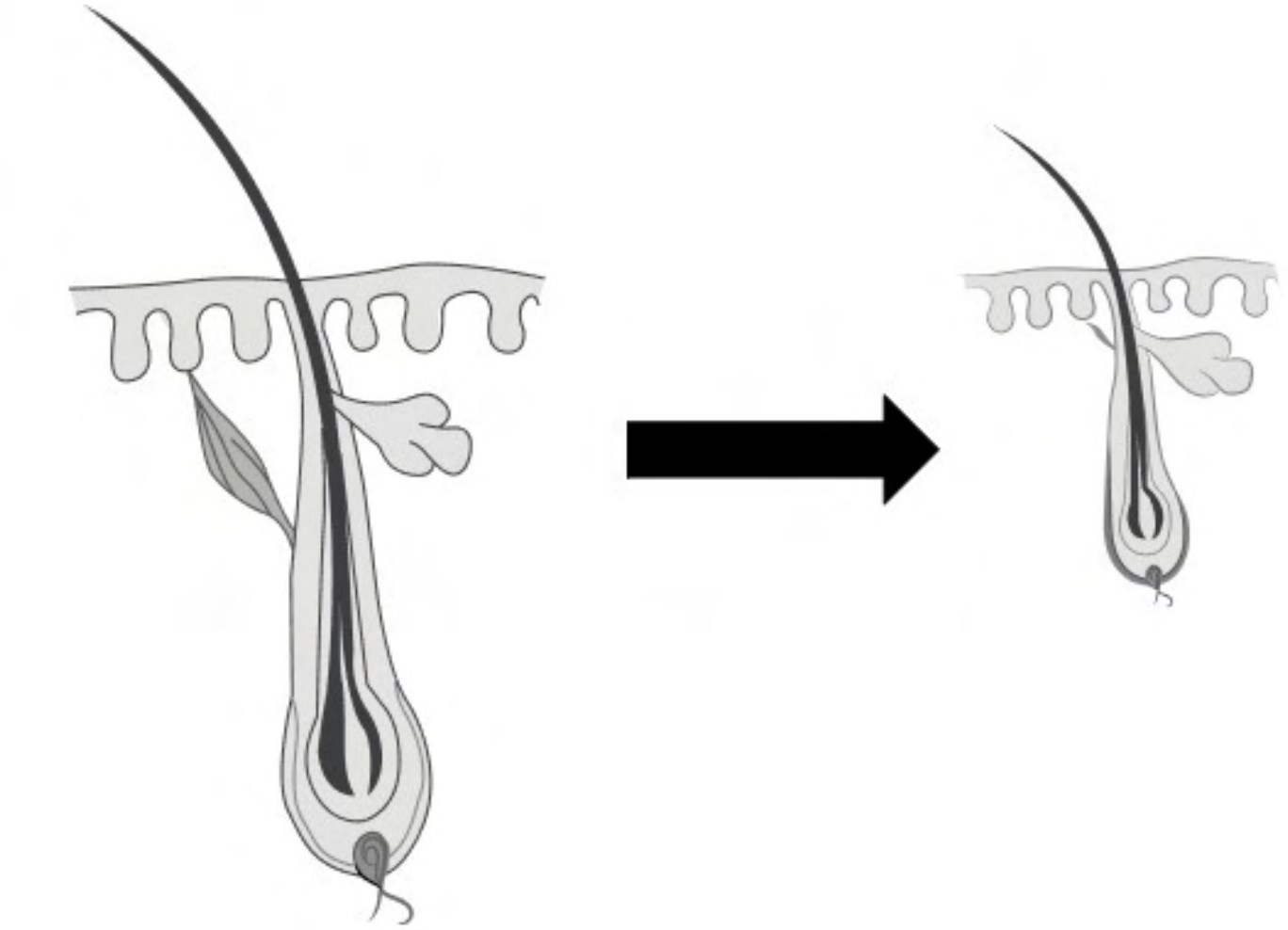
- The enzyme responsible for the production of prostaglandin F2-alpha is now deficient in NADPH
- This causes the reaction to create prostaglandin D2 instead
- Prostaglandin D2 is an agonist of PPAR-γ
- This triggers lipogenesis
- Prostaglandin D2 inhibits hair growth
- The size of sebaceous glands increase



- Agonism of PPAR-γ causes increased numbers of androgen receptors
- It also causes increased numbers of mitochondria in cells
- This causes overactive aerobic glycolysis and depletion of NADH
- The depletion of NADH interrupts ATP synthesis

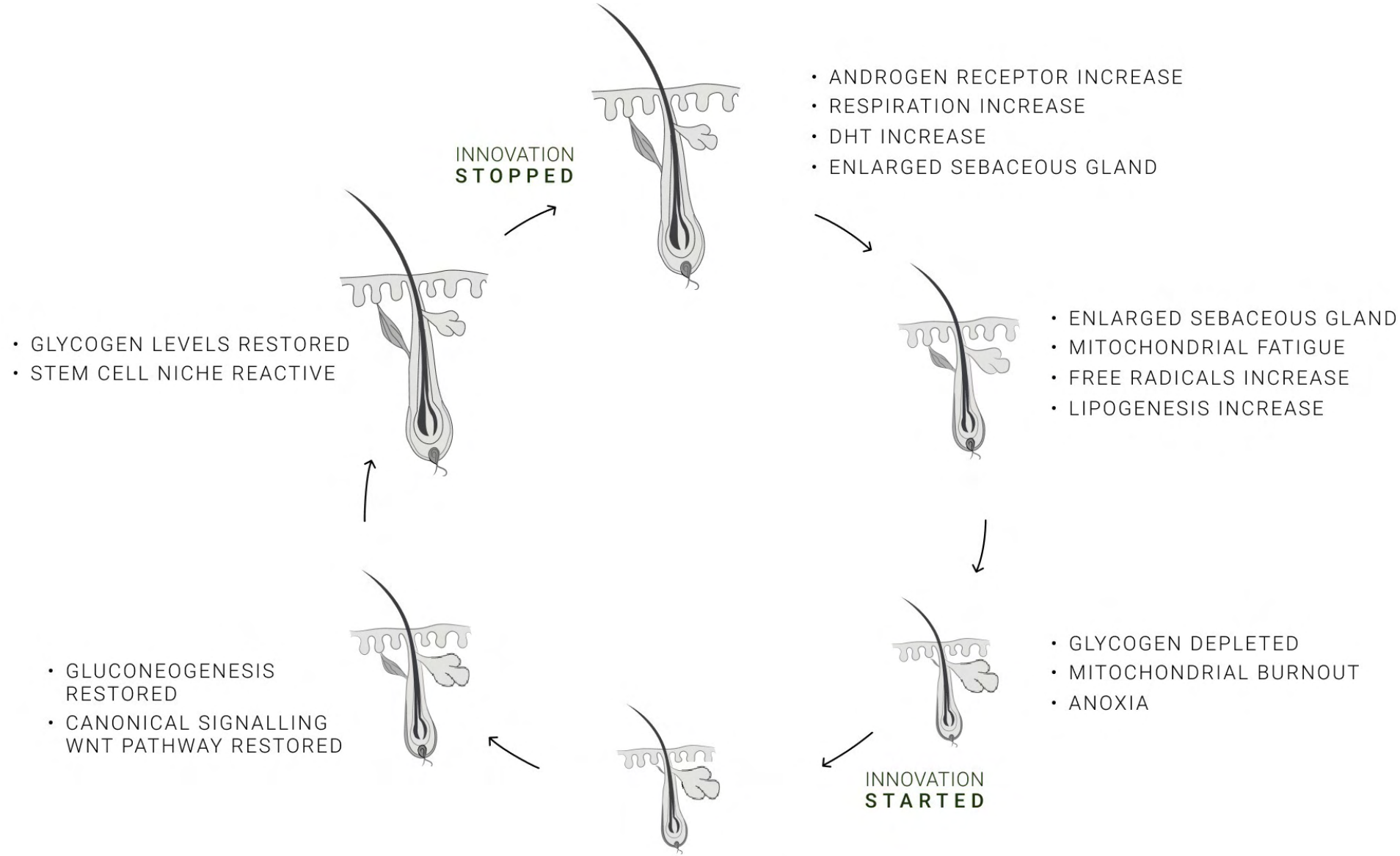


- Hair follicles miniaturize before becoming dormant
- The hair strands becomes discoloured
- The depth of the hair follicle is reduced
- The size of sebaceous glands increases



Section C:

Mechanism of System K11

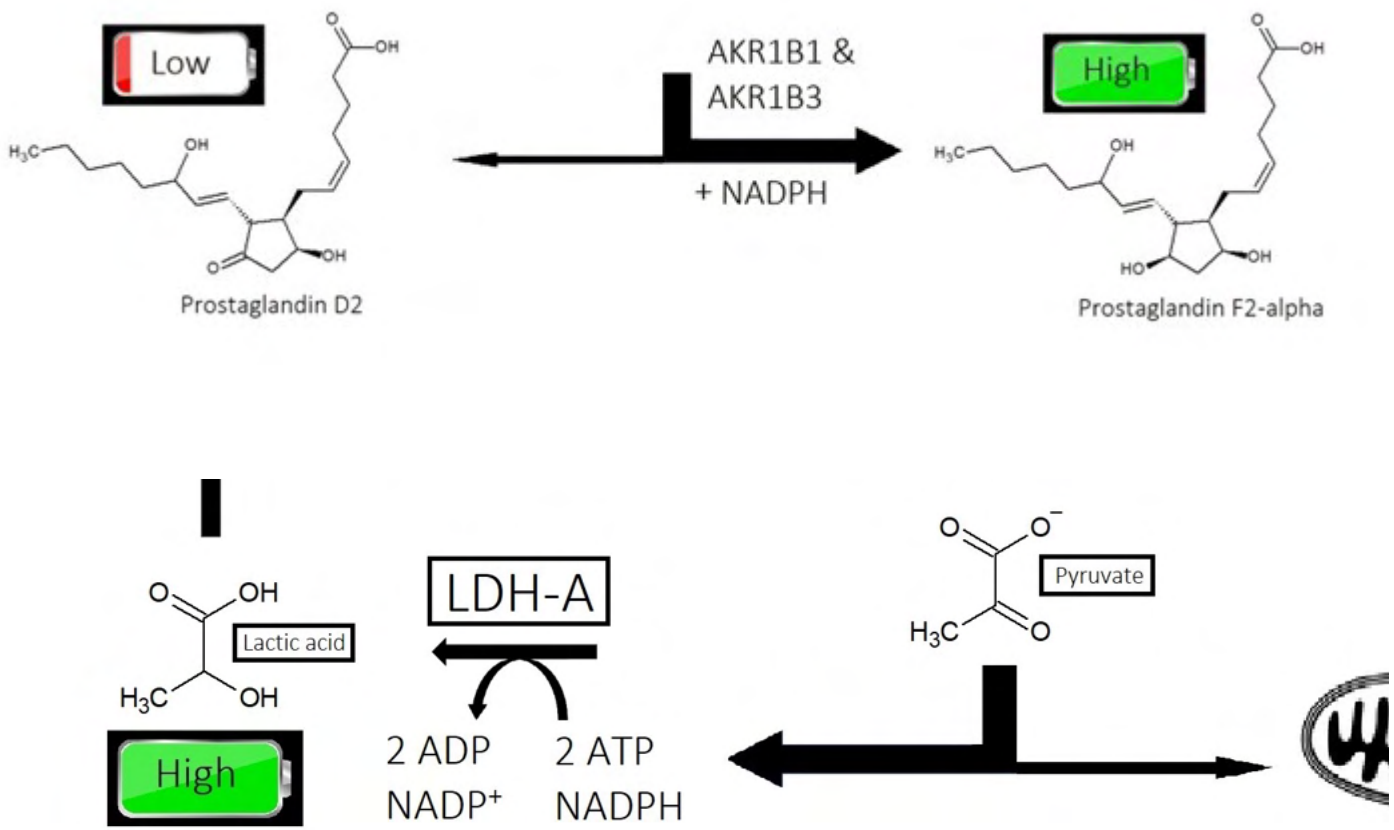


Mechanisms of System K11

1. Restores redox balance (increases NADH and NADH)
2. Restores liver function
    a) For conjugative removal of DHT
    b) For normalization of SHBG levels
3. Reduces prostaglandin D2
4. Restores the activity of 3α-HSD
5. Improves glucose levels (systemic)
6. Reduces the level of polyol metabolism
7. Reduces DHT
8. Reduces inflammation
9. Restores the ‘internal Cori cycle’ in hair follicles
10. Reduces mitochondrial fatigue
11. Reduced expression of TGF-β1
12. Restores electron transport chain
13. Addresses nutrient deficiencies

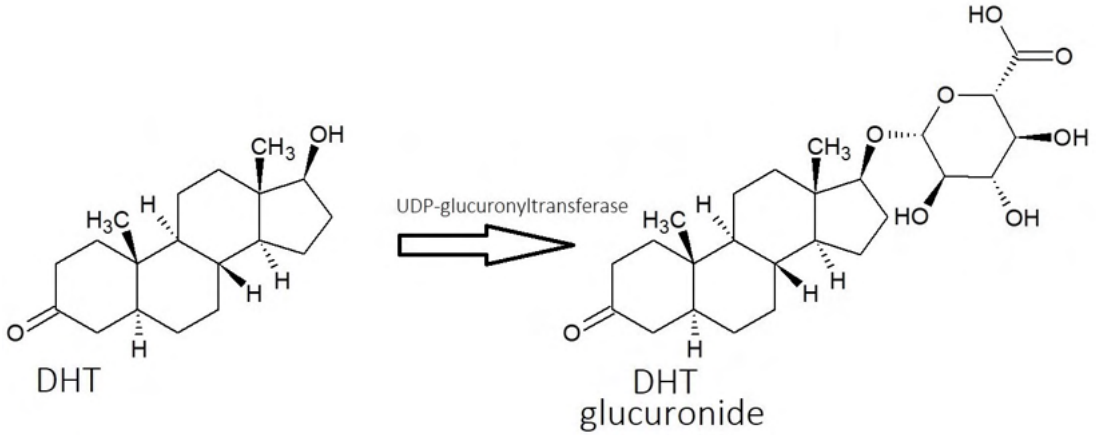
1) Ingredients that restore redox balance (increases NADH and NAD^+)

- Dihydroberberine
- Sulforaphane
- Magnesium (Mg^{2+})



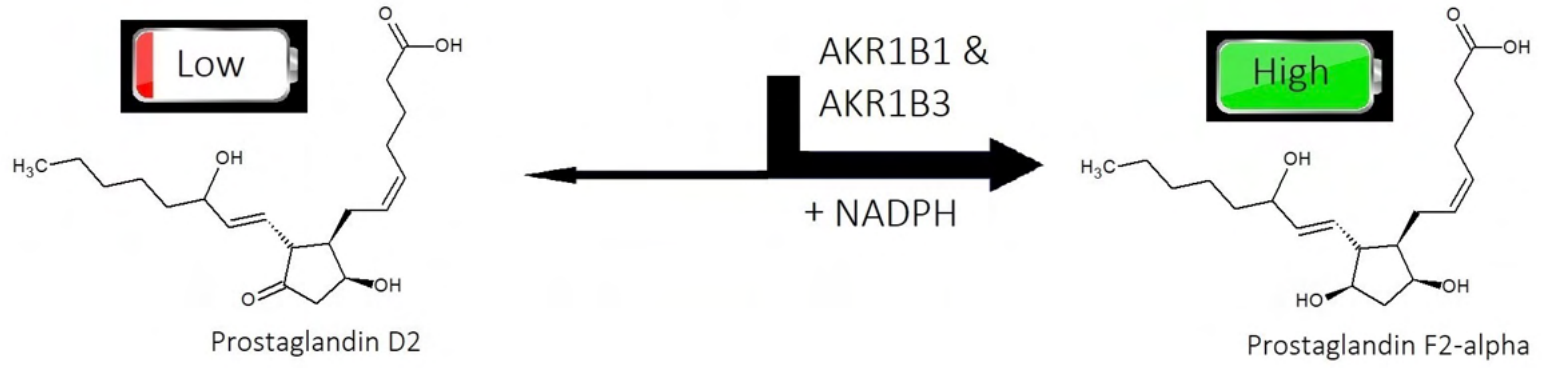
2) Ingredients that restore liver function

- Fenugreek
  - Normalizes SHBG
- Magnesium
- Gallactomannan
  - Gallactomannan is digested into short chain fatty acids, particularly butyrate, which is scientifically proven to improve liver function



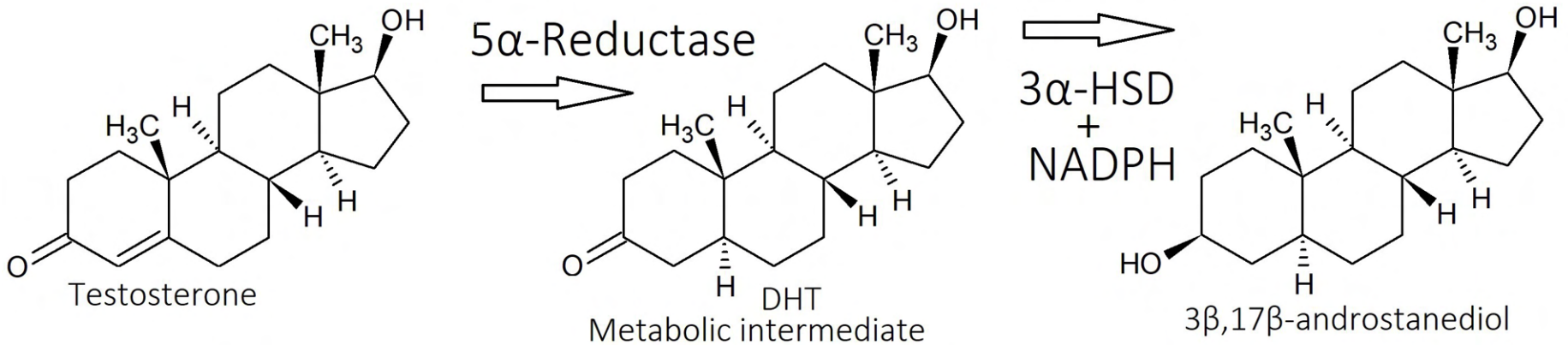
3) Ingredients that reduce prostaglandin D2

- Dihydroberberine
  - Dihydroberberine binds to AKR1B1, the same enzyme that produces PGD2. Other enzymes are available to produce PGF2-alpha
- Sulforaphane



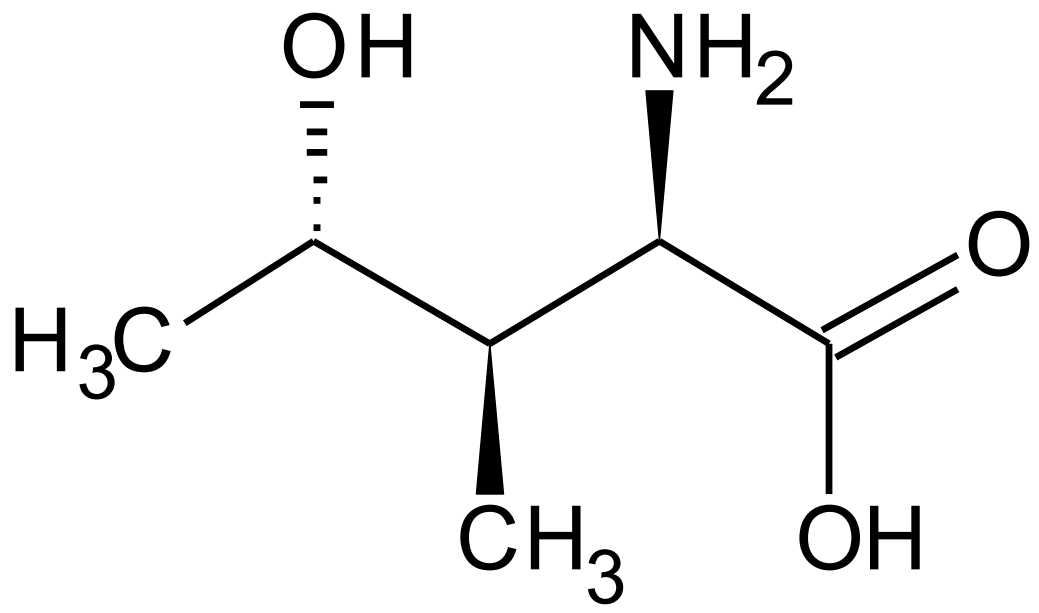
4) Ingredients that restore the activity of 3α-HSD

- Dihydroberberine
- Sulforaphane
  - Restores redox balance that potentiates DHT metabolism by 3α-HSD



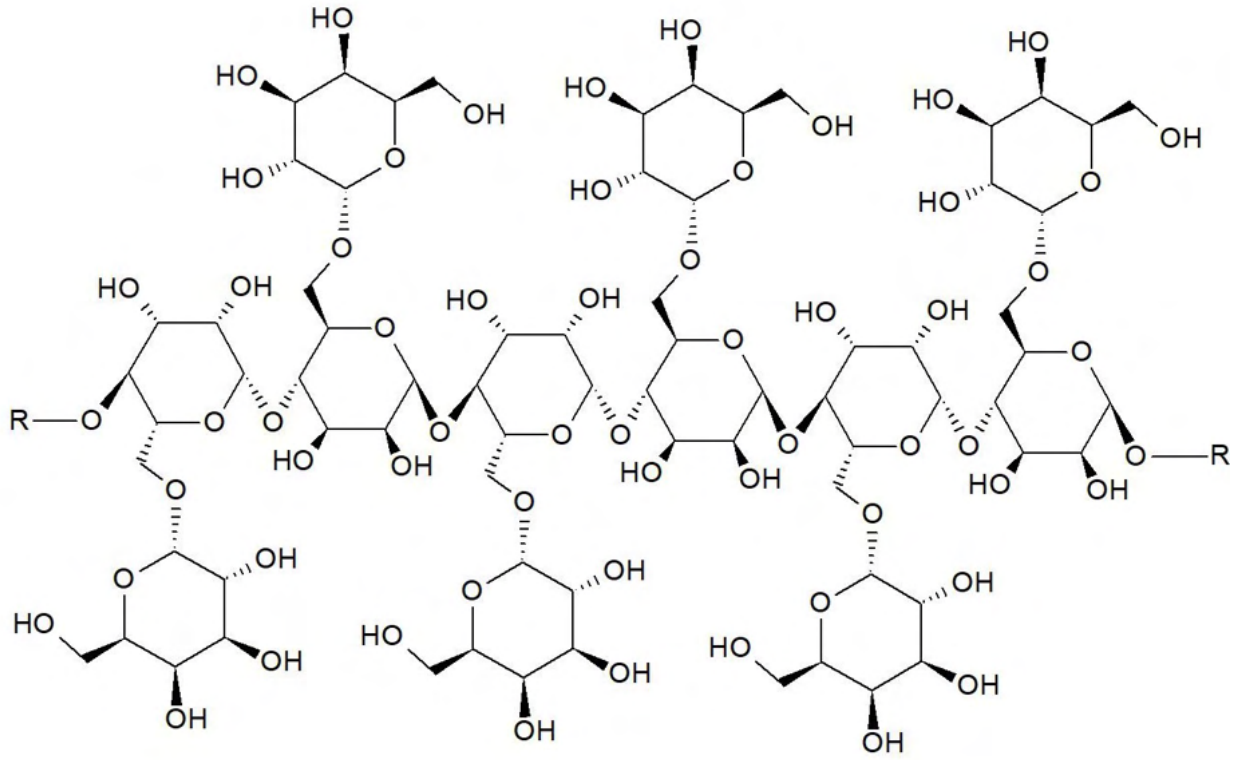
5) Ingredients that improve glucose levels (systemic)

- Dihydroberberine
- Fenugreek
  - Fenugreek includes 4-hydroxyisoleucine, an insulin sensitizer



5) Ingredients that improve glucose levels (systemic)

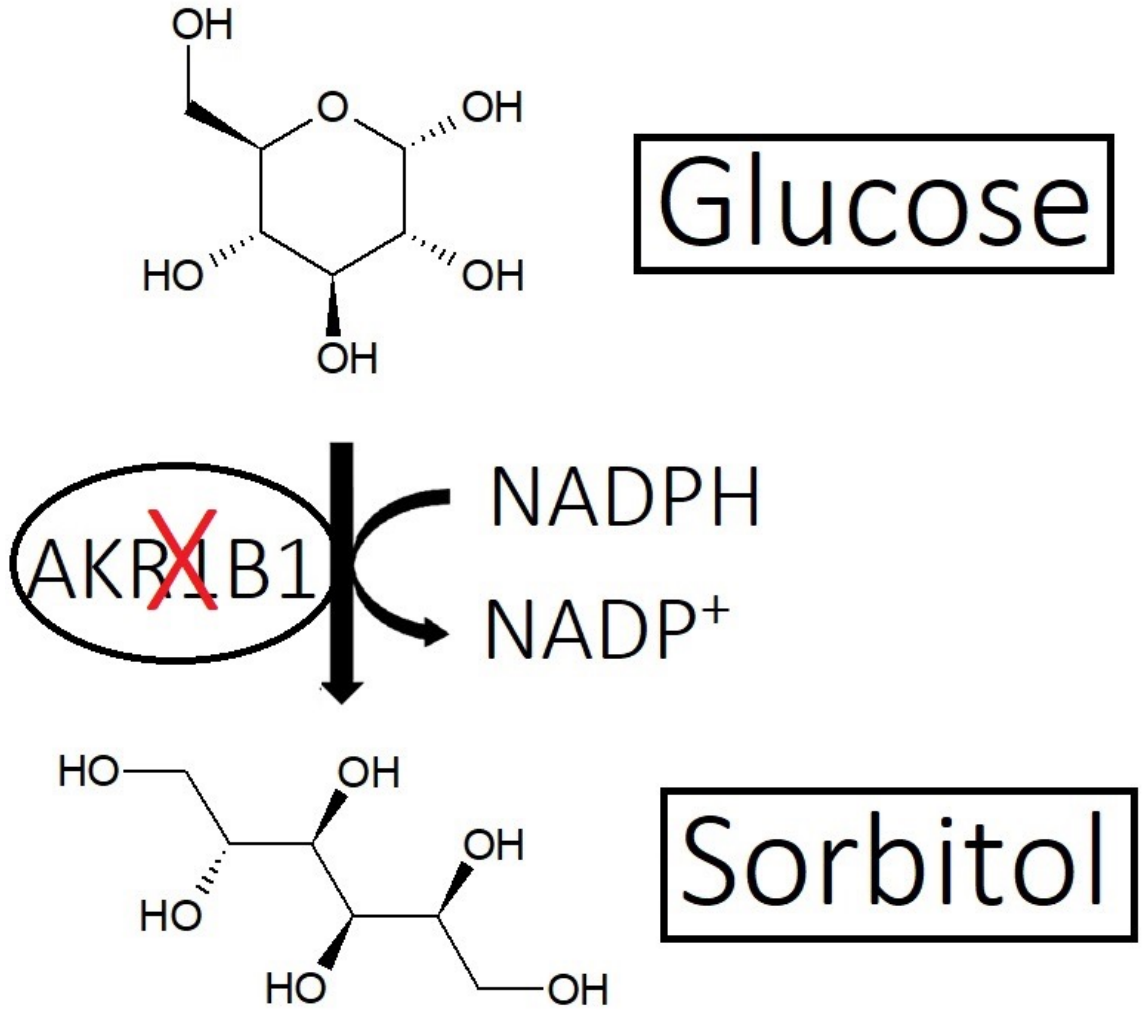
- Gallactomannan
  - A soluble dietary fibre that is digested into short chain fatty acids



Galactomannan (a-(1,6)-galactyl-β-(1,4)-linked mannose chain)

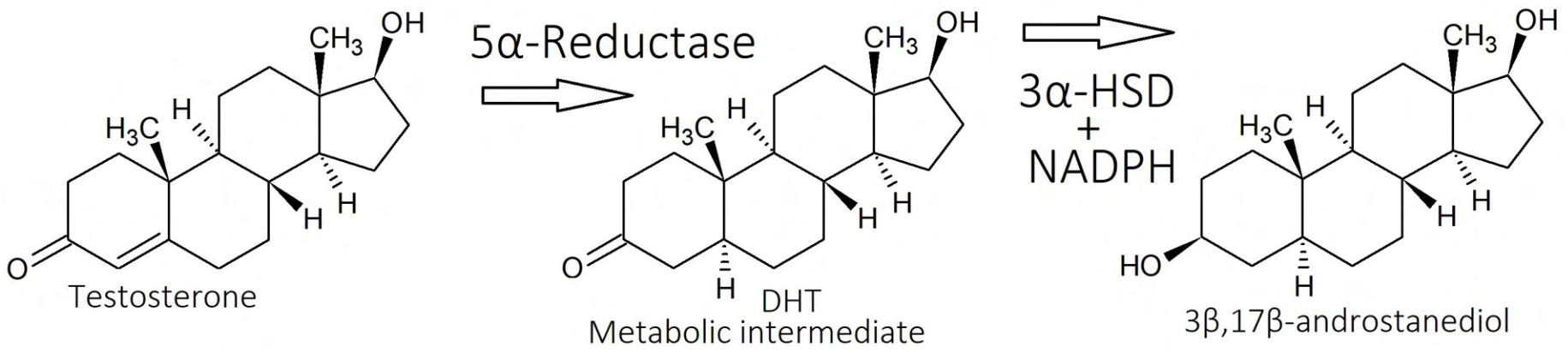
6) Ingredients that improve polyol metabolism

- Dihydroberberine
  - DHB binds to ARK1B1 (the same enzyme as in prostaglandin D2 synthesis, is also responsible for the polyol pathway)



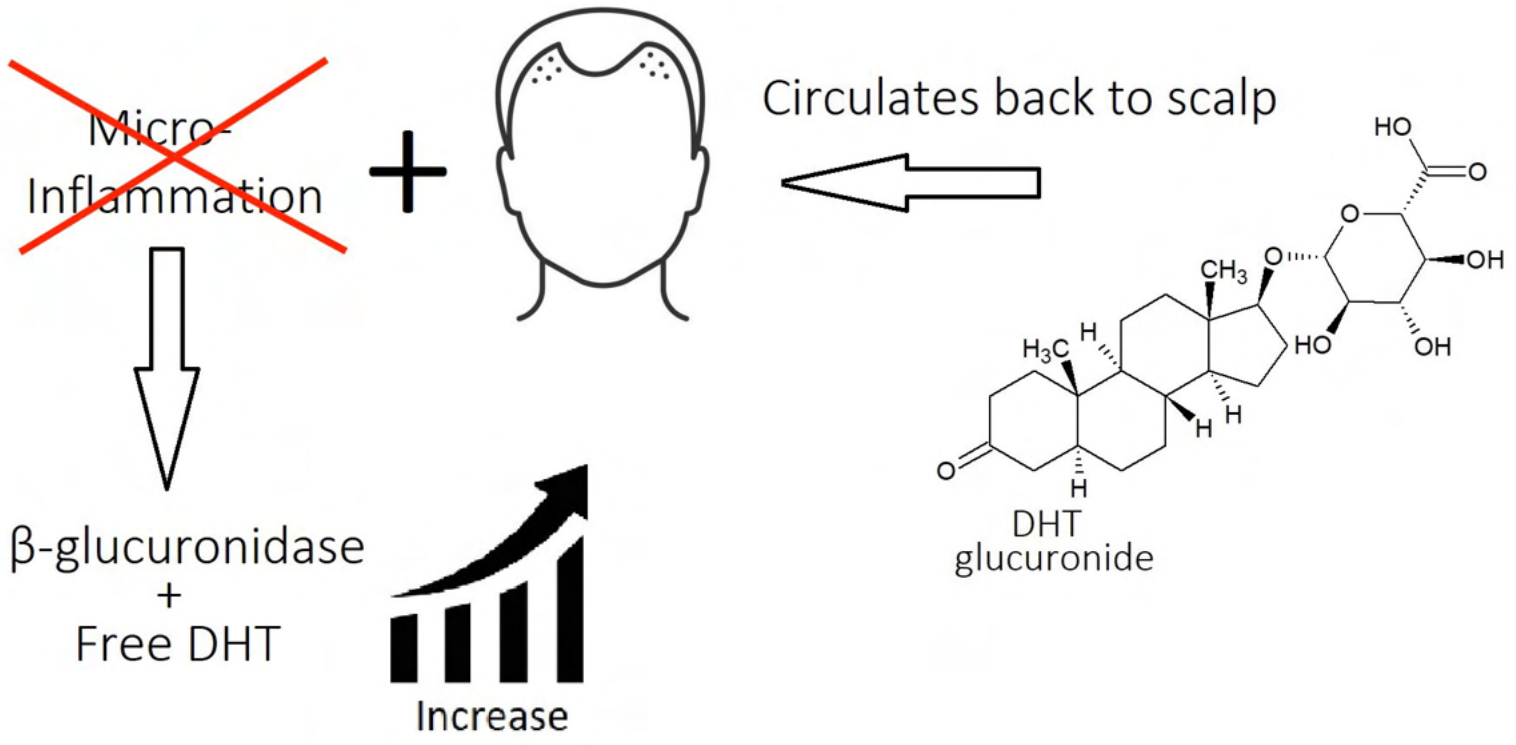
7) Ingredients that reduce DHT

- Dihydroberberine
- Sulforaphane
  - Restores NADPH & NAD+ to potentiate DHT metabolism by 3α-HSD
- Soy isoflavones
  - Mild 5α-reductase inhibition, boost liver function, restores redox balance



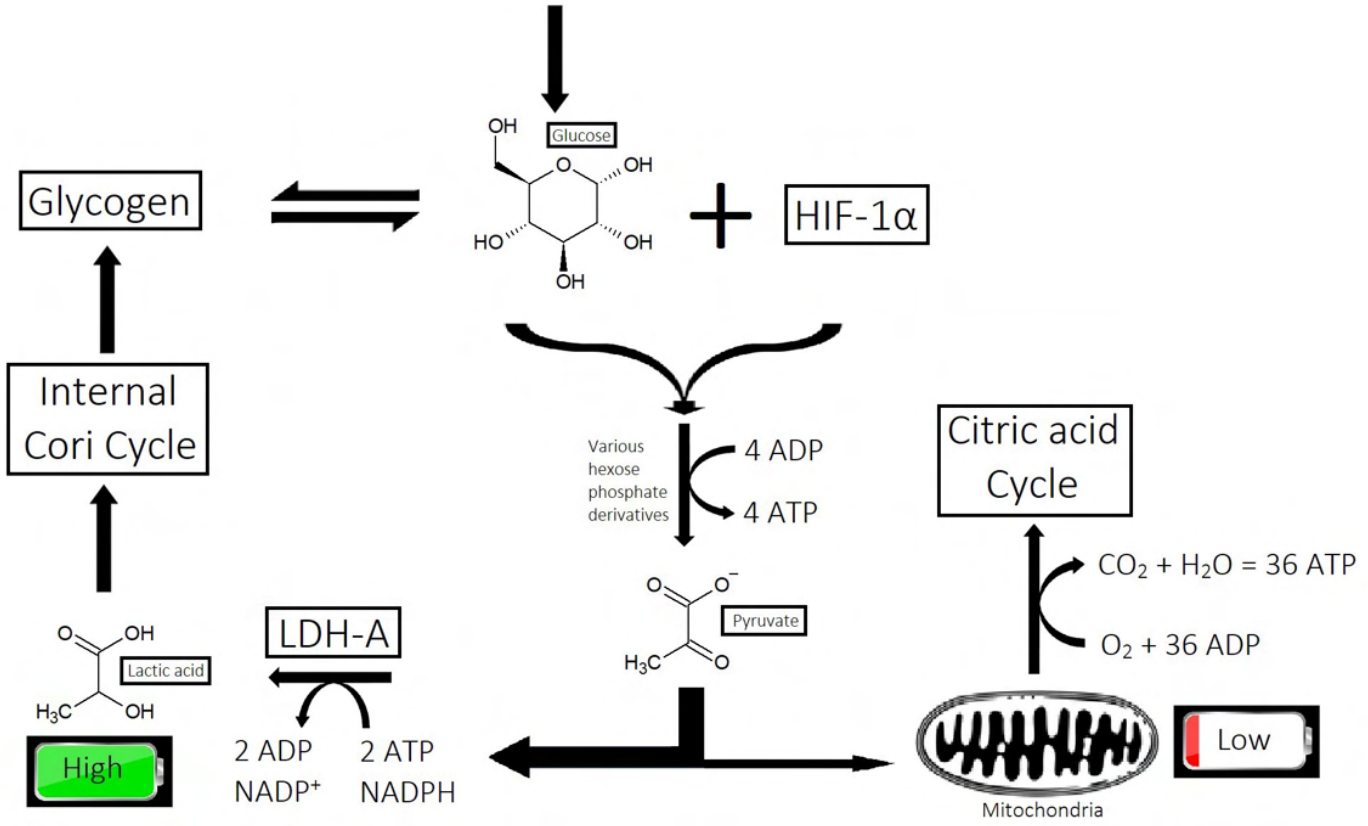
8) Ingredients that reduce inflammation

- Dihydroberberine is potently anti-inflammatory



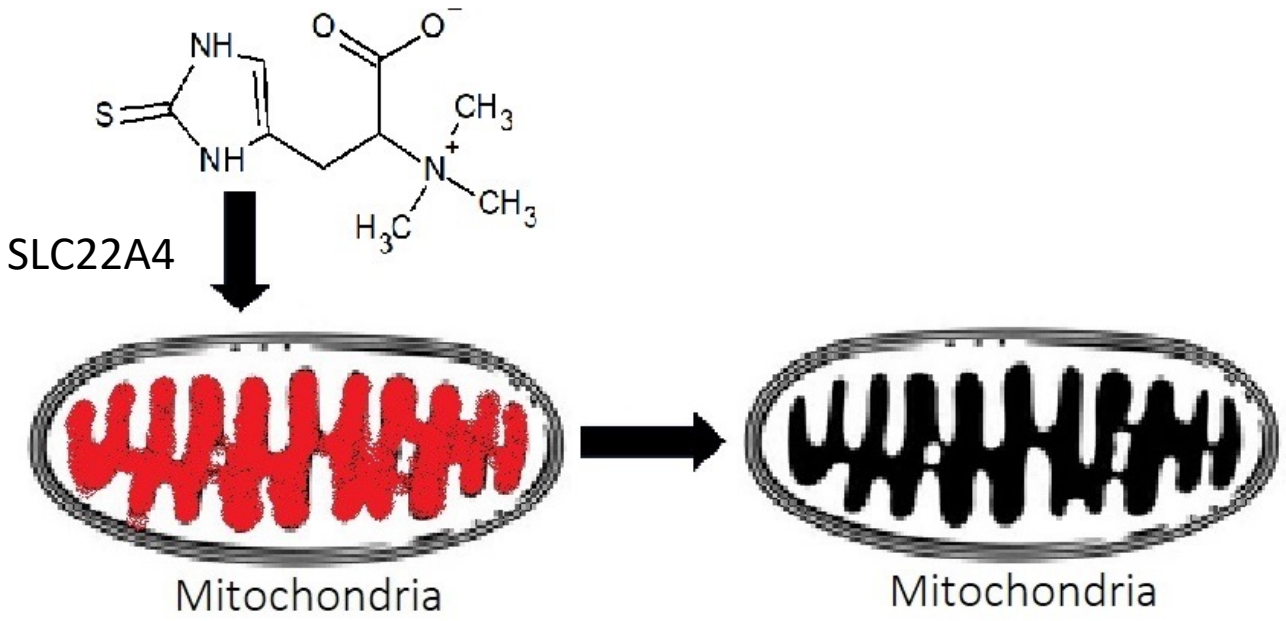
9) Ingredients that restore the ‘internal Cori cycle’ in hair follicles

- The same ingredients that reduce DHT
  - When DHT goes down, HIF-1α goes up
- Ingredients that improve glucose homeostasis



10) Ingredients that reduce mitochondrial fatigue

- Ergothioneine is a potent antioxidant that is actively transported to the mitochondria via ergothioneine transporter protein SLC22A4.
- Magnesium

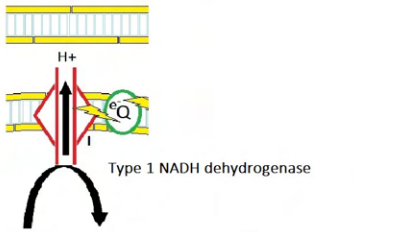


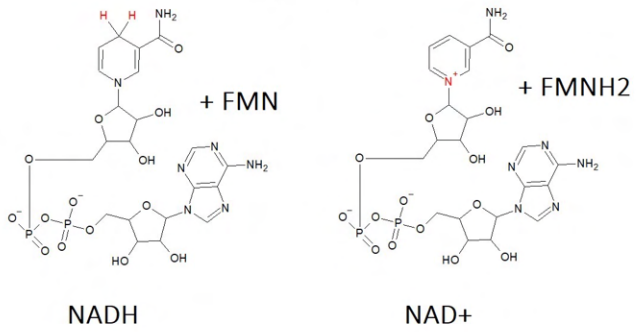
11) Ingredients that reduce expression of TGF-β1

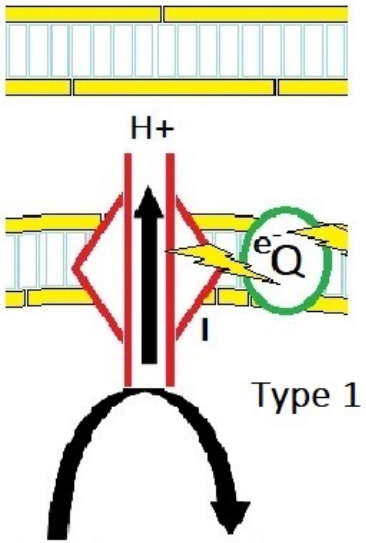
- Procyanidin B2 & B3 reduce cytoplasmic ROS

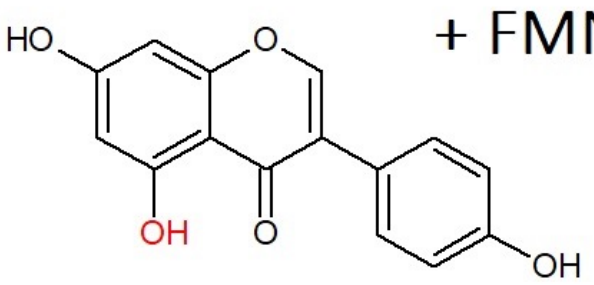
12) Ingredients that restore electron transport chain

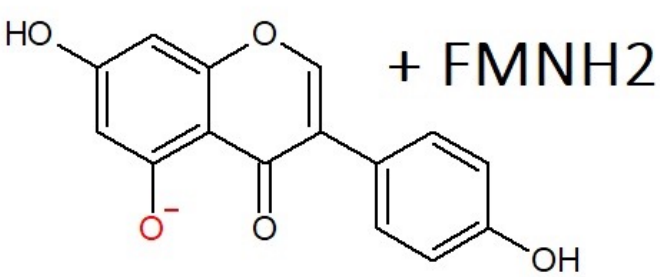
- Genistein
- Procyanidin B2
- Fenugreek











13) Ingredients that address nutrient deficiencies

- Magnesium
- Zinc
- Iron
- Iodine
- Vitamin D
- B vitamins
- Vitamin E