

Functional Herbal Therapy and Acne

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Our Topics

- Clinical features, pathophysiology, drivers and drug therapy of acne
- Does diet play a role in acne?
- Clinical evidence for herbs in acne, including topical application
- Traditional herbs for acne
- Therapeutic targets and herbal protocols informed by functional herbal therapy (FHT)
- Treatment summary



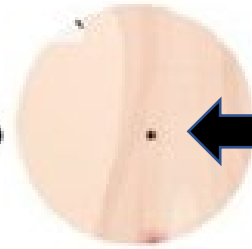
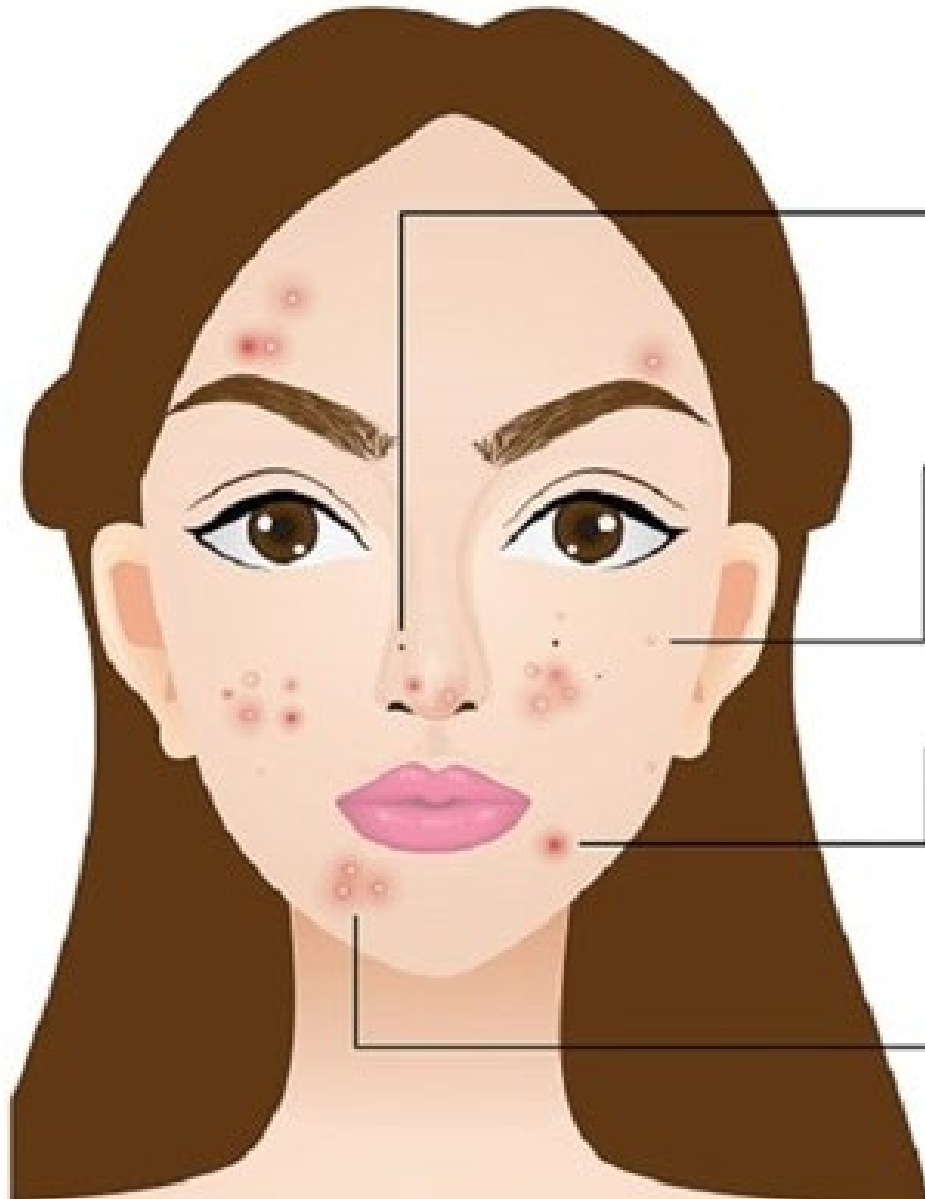
Clinical Features, Pathophysiology, and Drivers of Acne

Acne

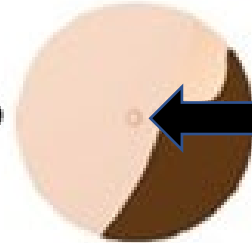
- The most common skin disease¹
- Affects 85% of teenagers, 42.5% of men, and 50.9% of women aged between 20 and 30 years¹
- Characterized by inflamed lesions or whiteheads and blackheads usually on the face, neck, back and chest²
- Cysts and scarring can occur in more severe cases²

Acne

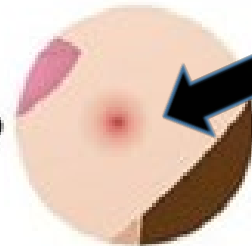
- “Acne is not a trivial skin disease. It is not a cosmetic condition. It is an inflammatory skin condition with a complex pathogenesis associated with a real, significant physical and psychological burden”
- But our knowledge of the pathogenesis of acne has deepened over the past decade
- “We still cling to the 4 major pathogenic factors: follicular hyperkeratinization, excess sebum, inflammation and *Cutibacterium acnes* (formerly *Propionibacterium acnes*)”
- “But as we study acne at the molecular level, we recognize the intricate and nuanced interplay between all of these factors”



Blackheads: Bumps on the skin that are yellow or black in color due to the pigmentation caused by the inner lining of hair follicles



Whiteheads: Similar bumps to blackheads but contain fluids



Papules: Small, painful red bumps



Pustules: Similar bumps to papules but are filled with white pus

Acne

Basic issues

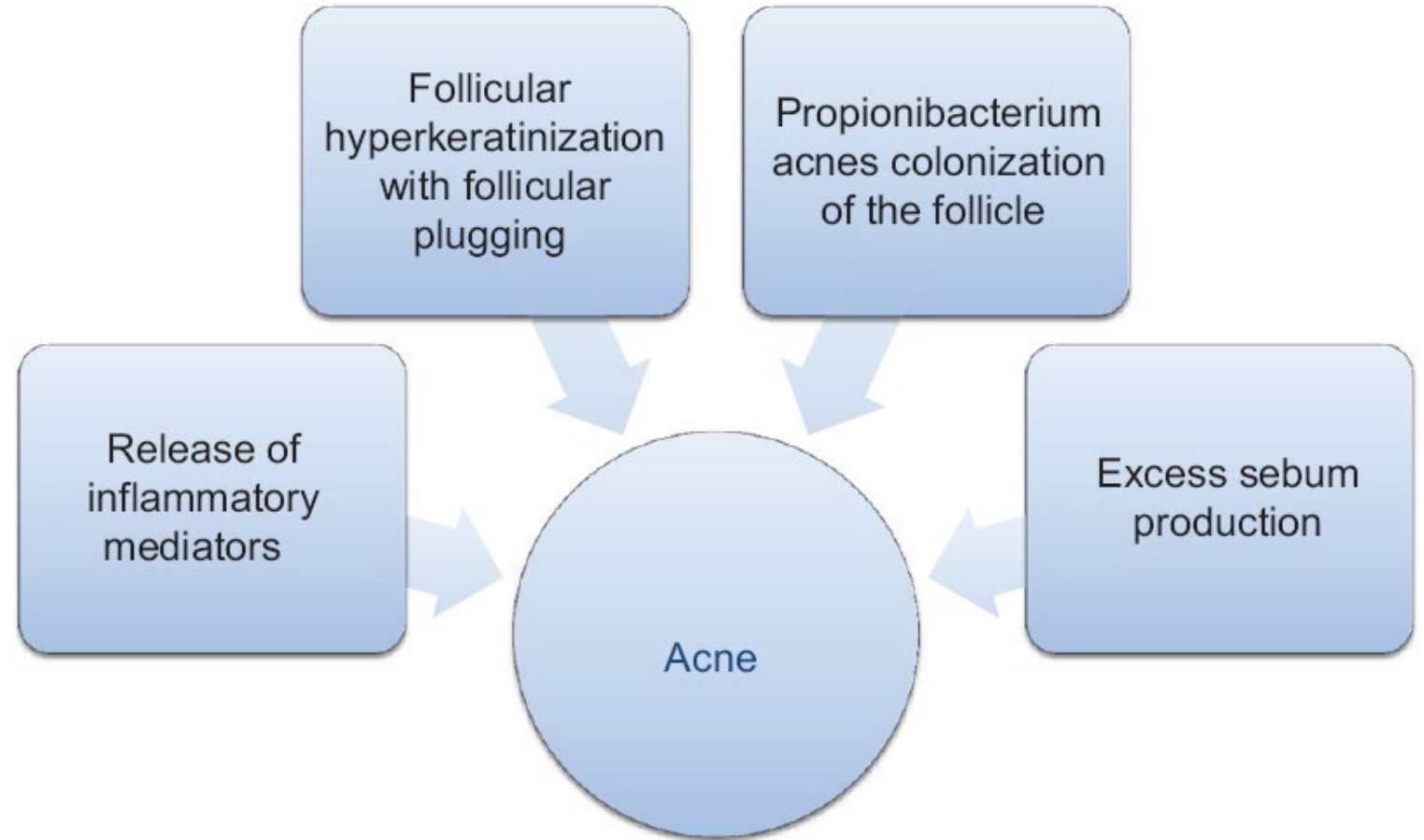
- May feature in some endocrine disorders, including polycystic ovarian syndrome (PCOS), Cushing's syndrome, androgen-secreting tumors and hyperinsulinemia
- Affects the sebaceous follicles (sebaceous glands associated with hair follicles)
- Linked to excess hormone production (androgens, growth hormone, insulin-like growth factor 1 [IGF-1], insulin, glucocorticoids)

Acne

Pathophysiology

- Hyperseborrhea, linked to hyperandrogenism (premenstrual acne, teenage acne)
- Abnormal keratinization of the pilosebaceous duct
- *Cutibacterium acnes* (*C. acnes*) proliferation in the pilosebaceous unit
- Immune inflammatory response against *C. acnes*
- Cutaneous microbiome (resident microbes on the skin) imbalance

Acne - Pathophysiology



Acne

Role of *Cutibacterium acnes*

- Sebum and keratin accumulation allows *C. acnes* and other **anaerobic** microorganisms to proliferate¹
- *C. acnes* stimulates sebaceous lipogenesis²
- *C. acnes* increases keratinocyte expression and inflammatory cytokines²
- *C. acnes* initiates innate immune responses²

1. Clayton RW, Göbel K, Niessen CM et al. *Br J Dermatol*. 2019; **181**(4): 677-690. doi: 10.1111/bjd.17981. PMID: 31056753

2. Platsidaki E, Dessinioti C. *F1000Res*. 2018; 7. pii: F1000 FacultyRev-1953. doi: 10.12688/f1000research.15659.1. PMID: 30613388

Acne: Role of *Cutibacterium acnes*

But it's complex...

- No quantitative differences in *C. acnes* of the skin of patients with acne compared with controls
- But *C. acnes* biofilms are more frequent and different phylotypes may induce distinct immune responses in acne
- *C. acnes* also plays a further important role in the homeostasis of the skin's microbiome, interacting with other cutaneous commensal or pathogenic microorganisms



Acne

Cutaneous microbiome

- Affected by internal (genetic, hormonal) and external factors (cosmetics, soaps, diet)
- Modifications to the natural skin microbiome trigger skin inflammation leading to acne (dysbiosis of the skin)
- “Rebalancing the natural microbiome of the skin by restoring the natural skin barrier, limiting the proliferation of *C. acnes* on the skin by using topical antibacterials which do not cause resistance, and regulating quantity and quality of sebum will be the main acne treatment challenges in the future”

Androgen issues

- Enzyme 5-alpha reductase (5α-R) is found in skin, hair follicles and sebaceous glands
- Testosterone is reduced to dihydrotestosterone (DHT) by 5α-R isozymes
- DHT is the preferred ligand for androgen receptor transactivation: acne can be viewed as a dermatological manifestation of excess testosterone, DHT and a higher androgen receptor density
- Increasing sex hormone binding globulin (SHBG) can reduce androgen effects in acne



**Does Diet Play a
Role in Acne?**

Diet and Acne

- Acne is virtually absent in populations consuming paleolithic diets¹
- Androgens, hormonal mediators (including IGF-1) are found in dairy products, and can survive processing¹
- These factors can contribute to excess sebum production in acne¹
- Following a low GL diet, acne improvement was observed in male patients²
- A low GI and GL diet decreased IGF-1 in adults with moderate and severe acne in a 2-week trial³

1. Bhat YJ, Latief I, Hassan I. *Indian J Dermatol Venereol Leprol.* 2017; **83**(3): 298-306. doi: 10.4103/0378-6323.199581. PMID: 28195079

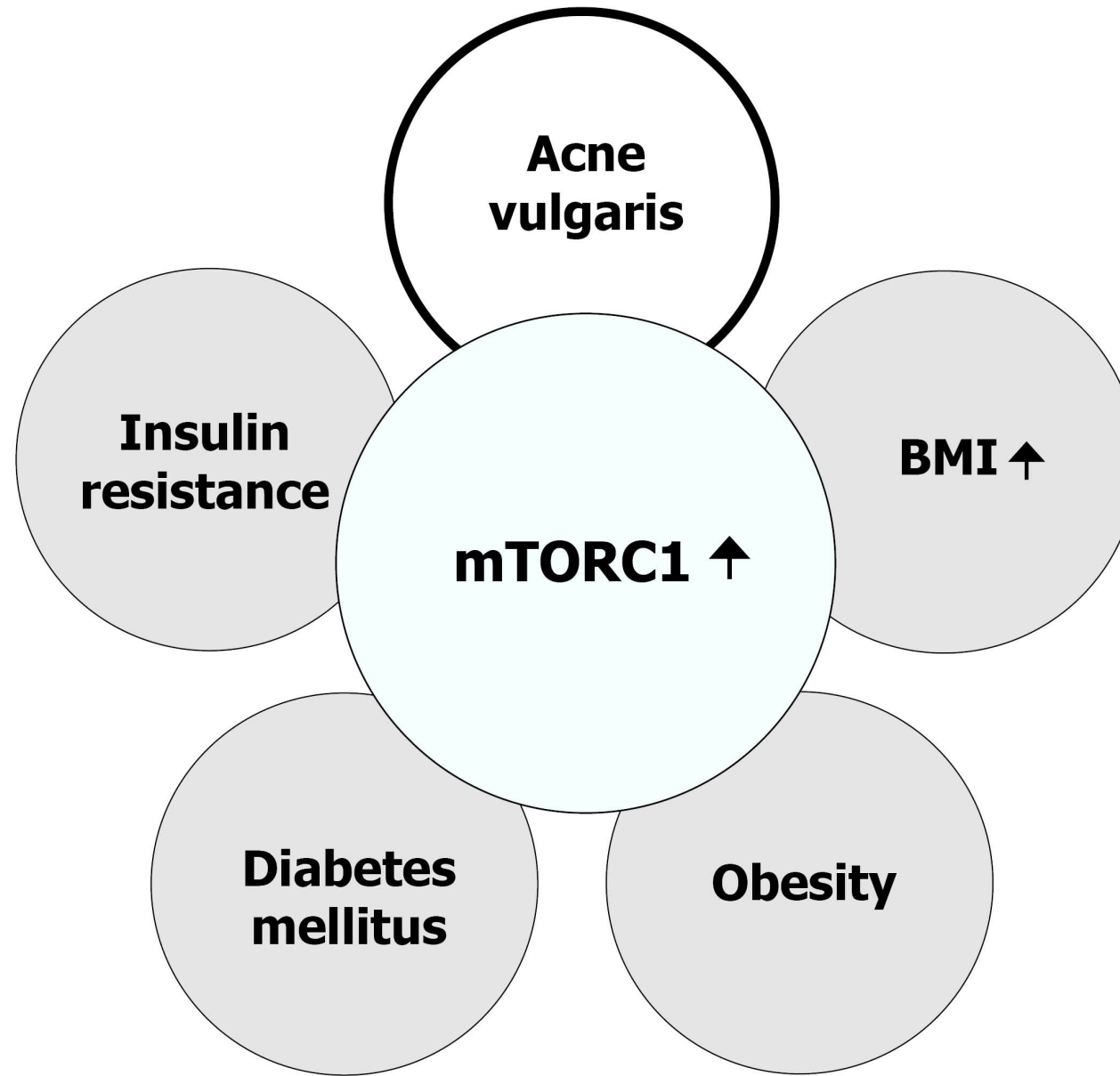
2. Smith RN, Mann NJ et al. *Am J Clin Nutr.* 2007; **86**(1): 107-15. PMID: 17616769

3. Burris J, Shikany JM et al. *J Acad Nutr Diet.* 2018; **118**(10): 1874-85. doi: 10.1016/j.jand.2018.02.009. PMID: 29691143

Hyperseborrhea

- Linked to Western diets (high GL carbohydrates, saturated fats and dairy products)
- Sebocytes use the same regulatory mechanisms for lipogenesis and inflammation
- Leptin is involved: regulates sebocyte lipogenesis via up-regulation of mammalian target of rapamycin complex 1 (mTORC1) signaling, thereby increasing sebum production







Acne vulgaris: The metabolic syndrome of the pilosebaceous follicle

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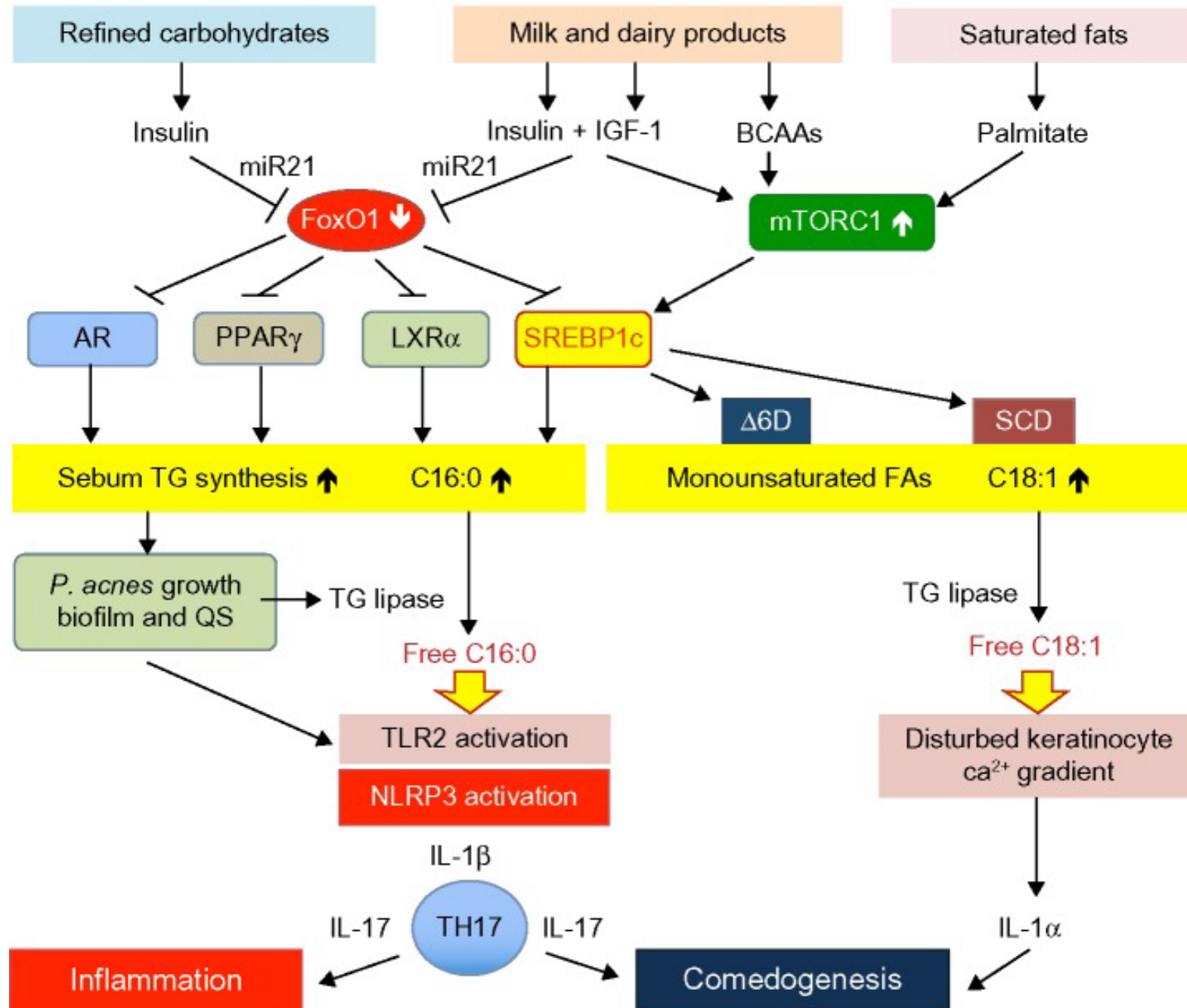
Abstract *Acne vulgaris* is an epidemic inflammatory disease of the human sebaceous follicle and represents the most common skin disease affecting about 85% of adolescents in Westernized populations. *Acne vulgaris* is primarily a disease of wealthy countries and exhibits higher prevalence rates in developed compared with developing countries. No acne has been found in non-Westernized populations still living under Paleolithic dietary conditions constraining hyperglycemic carbohydrates, milk, and dairy products. The high prevalence rates of adolescent acne cannot be explained by the predominance of genetic factors but by the influence of a Western diet that overstimulates the key conductor of metabolism, the nutrient- and growth factor-sensitive kinase mTORC1. Increased mTORC1 activity has been detected in lesional skin and sebaceous glands of acne patients compared with acne-free controls. Increased mTORC1 signaling is a characteristic feature of insulin resistance, obesity, type 2 diabetes mellitus, cancer, and neurodegenerative diseases. *Acne vulgaris* is a family member of mTORC1-driven diseases of civilization and represents the MetS of the sebaceous follicle.

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No acne has been found in non-Westernized populations still living under Paleolithic dietary conditions constraining hyperglycemic carbohydrates, milk, and dairy products

The high prevalence rates of adolescent acne cannot be explained by the predominance of genetic factors but by the influence of a Western diet that overstimulates the key conductor of metabolism, the nutrient- and growth factor-sensitive kinase mTORC1

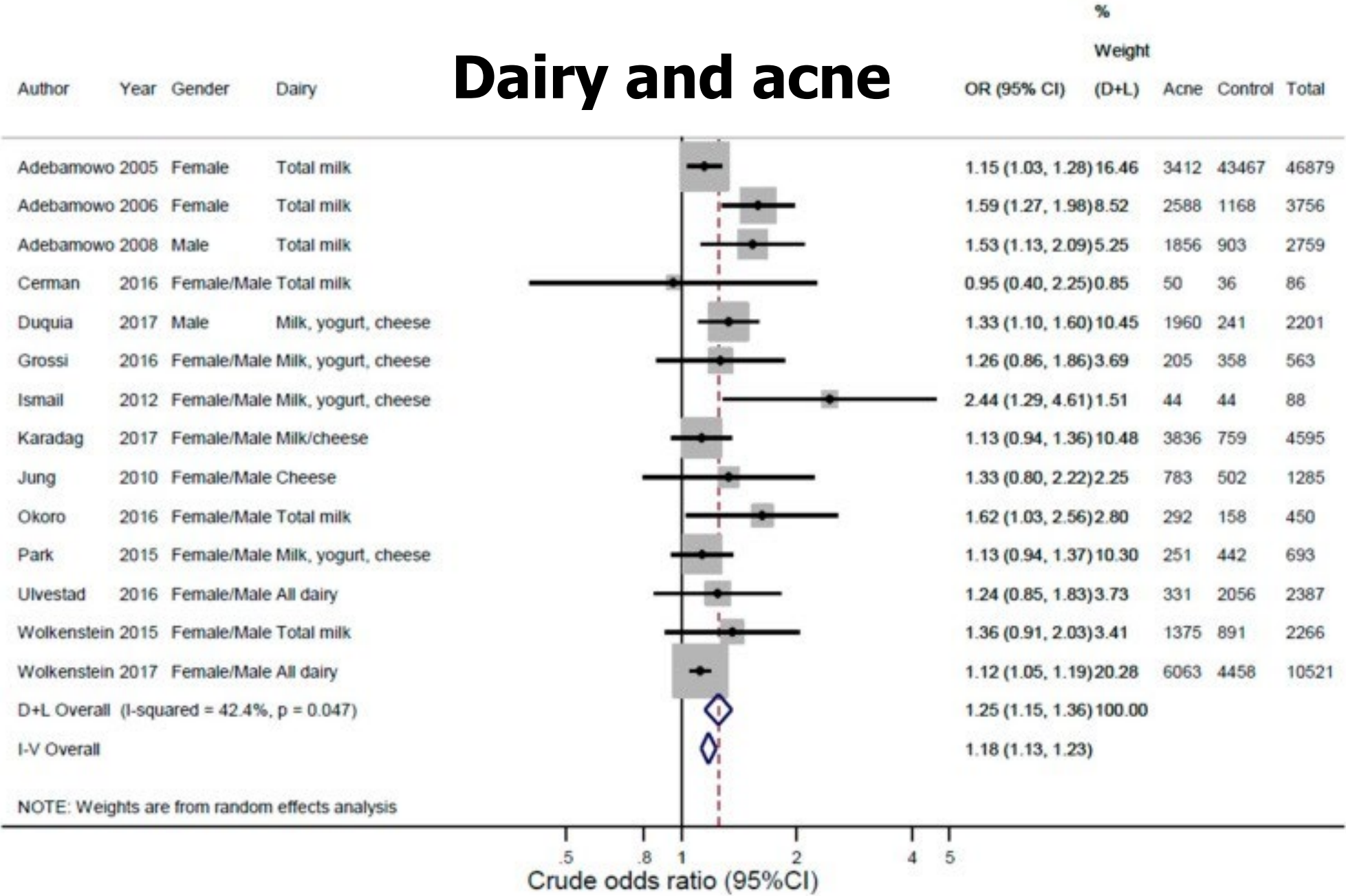
Western diet



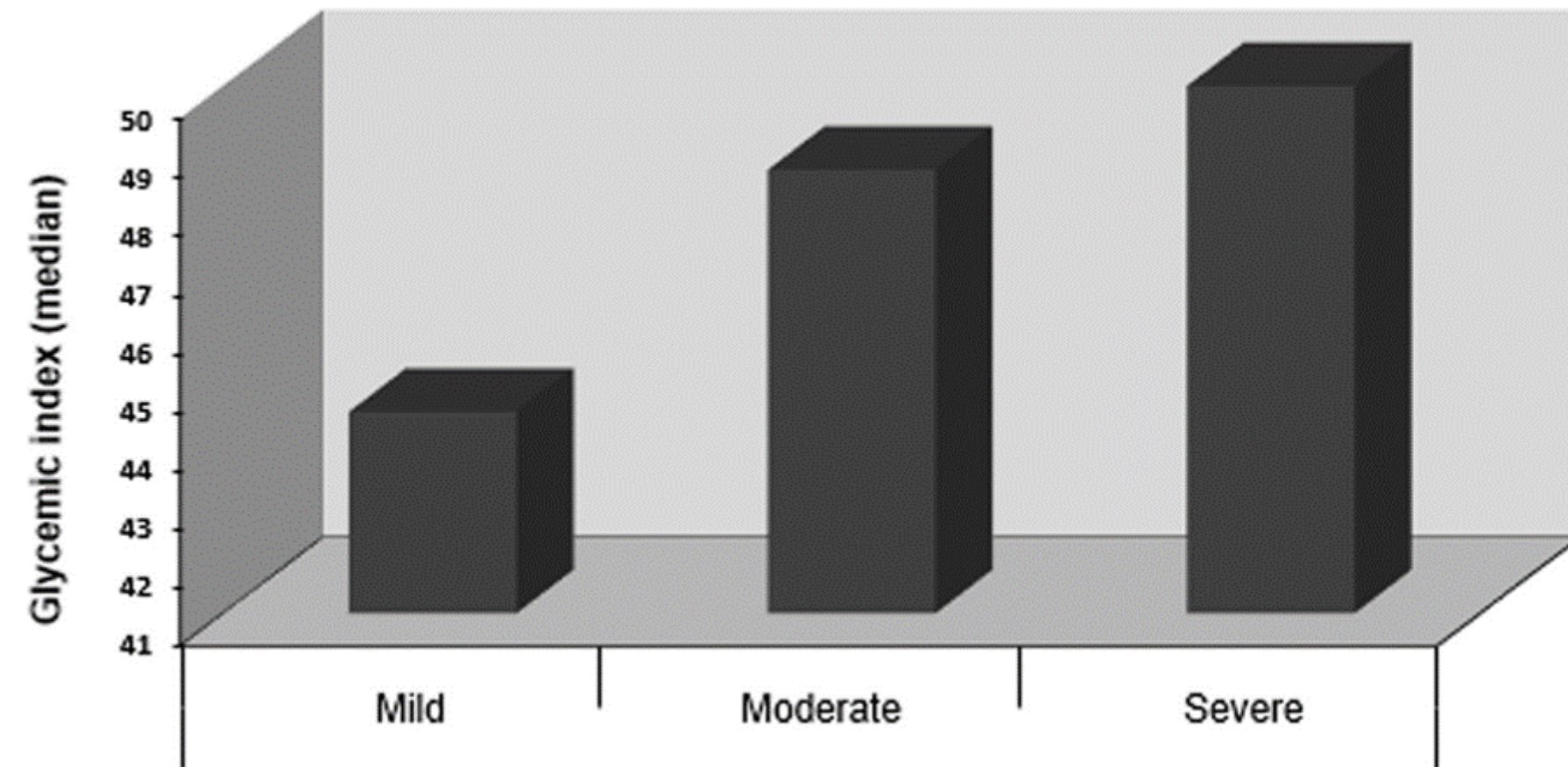
Abbreviations: IGF-1, insulin-like growth factor 1; BCAAs, branched-chain amino acids; miR21, microRNA-21; FoxO1, forkhead box class O1; mTORC1, mechanistic target of rapamycin complex 1; AR, androgen receptor; PPAR γ , peroxisome proliferator-activated receptor-gamma; LXR α , liver X receptor-alpha; SREBP1c, sterol response element binding protein 1c; $\Delta 6D$, $\Delta 6$ -desaturase; SCD, stearoyl-CoA desaturase; TG, triglyceride; *P. acnes*, *Propionibacterium acnes*; QS, quorum sensing; C16:0, palmitic acid; C18:1, oleic acid; TLR2, toll-like receptor 2; NLRP3, Nod-like receptor family, pyrin domain containing 3 inflammasome; IL-1 β , interleukin-1beta; Th17, Th17 T-cell; IL-17, interleukin-17; IL-1 α , interleukin-1alpha

Melnik BC. *Clin Cosmet Investig Dermatol*. 2015; **8**: 371-88. doi:10.2147/CCID.S69135. PMID: 26203267

Dairy and acne



GI of the Diet and Acne Severity



CAPSULE SUMMARY

- High-glycemic-index/-load diets have been implicated in acne pathogenesis.
- Hypoadiponectinemia associated with a high-glycemic-index/-load diet may augment the inflammatory response in patients with acne.
- A low-glycemic-index/-load diet may have therapeutic potential in acne management.

Diet and Acne

Foods identified as acne triggers in various studies include:

- Refined grains and sweets
- Dairy products
- Fast food
- Chocolate, including dark chocolate and cocoa powder
- Whey protein

Diet a significant factor in acne outbreaks, finds pioneering new study



Acne and the exposome

By Dr. Liji Thomas, MD Oct 14 2019

A new study presented at the 28th EADV Congress in Madrid has demonstrated the effects of exposure to various factors on acne, both internal and external. An unhealthy diet, a high level of stress, and extreme skincare routines were the most significant factors related to acne breakouts. This is the first-ever study to look at so many factors in this way.

The study shows that almost 43% of people with acne consume milk products, and 11% eat whey protein daily, compared to 39% and 7% respectively of those who don't. Similarly, more people with acne drink syrups or juices (36%), eat chocolates or pastry (37%), and have sweets (30%), compared to the rest (31%, 28%, and 19%, respectively).

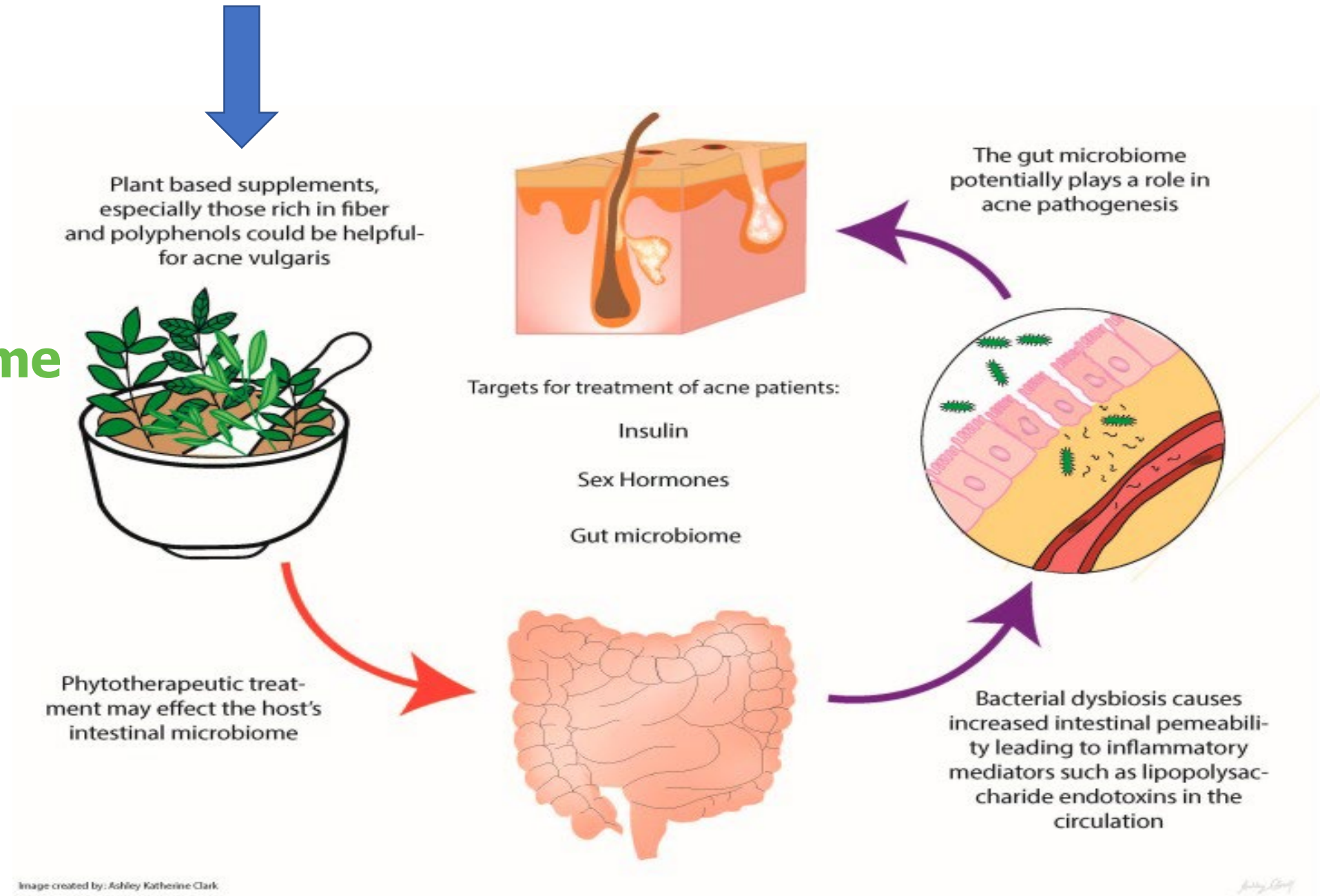
Anabolic steroid use occurs in about 12% of those with acne compared to 3% of those without. Polluted air is another contributor, as is stress – but not tobacco use.

From a mainstream dermatology journal

Key Points for Dietary Counseling of Acne Patients

- Data-driven evidence supports a role for high GI/GL diets and dairy products (particularly whole, low-fat, and skim milk) as exacerbating factors for acne vulgaris; however, patients should be advised that dietary factors do not independently cause acne
- There is little evidence that chocolate without accompanying sugar or milk is a notable factor in acne development
- It should be noted that changes in acne due to any pharmaceutical treatment or dietary changes are likely to take at least 10 to 12 weeks
- Acne patients should be encouraged to discontinue any whey protein supplements they might be taking

Gut microbiome



Evidence-based Diet for Acne

- Low in sugar (including dried fruits and fruit juices)
- Low in saturated fats
- Low in glycemic index (GI) and load (GL)
- Dairy free (all animal sources)
- Lower in BCAAs and general animal protein (IGF-1 aspect)
- Rich in fiber





Clinical Evidence for Ingested Herbs in Acne

Green Tea (*Camellia sinensis*)

- Decaffeinated green tea extract assisted in reducing inflammatory acne lesions (moderate to severe) in 64 post-adolescent women (aged 20-45) in a randomized double blind, placebo-controlled clinical trial (RDBPCT)
- The daily dose used was 1500 mg extract (containing 856 mg epigallocatechin gallate, EGCG), which significantly reduced lesions on the chin, nose and perioral area
- Effects were modest



Chaste Tree (*Vitex agnus-castus*)

- In a 2-year, controlled, open-label trial which included 161 acne patients, treatment with chaste tree (40 drops/day tincture for 4 to 6 weeks followed by 30 drops/day) for a minimum of 3 months in conjunction with a mild topical disinfectant resulted in an improvement for 70% of patients
- This result was significantly more effective than standard therapy
- The mechanism for the beneficial effect of chaste tree on acne may be due to a mild anti-androgenic effect



Milk Thistle (*Silybum marianum*)

- RCT (n=60) in acne vulgaris: patients were divided into three groups of 20: silymarin (140 mg/day; Group 1), doxycycline (100 mg/day; Group 2) and both (Group 3) for two months
- Response was monitored every month and lesions were evaluated using photography and two methods of Global Acne Grading System (GAGS) and Acne Severity Index (ASI)
- Response to silymarin was not significantly different to doxycycline in the GAGS index ($p = 0.260$), but was less in the ASI ($p = 0.021$)
- Although the improvement was more favorable in the combination group, it did not achieve statistical significance



Before (a) and after (b) images of patients with different severity of acne vulgaris who were treated with silymarin for two months

Licorice (*Glycyrrhiza* spp.) and White Peony (*Paeonia lactiflora*)

- Combination of Peony root and licorice root is used in Chinese and Japanese traditional medicine (SKT or TJ-98)
- SKT (equivalent to 6 g/day of dried Peony root and 6 g/day of dried Licorice root) for 12 weeks significantly decreased serum free testosterone compared to baseline values in women with acne vulgaris
- Treatment also significantly decreased the number of comedones





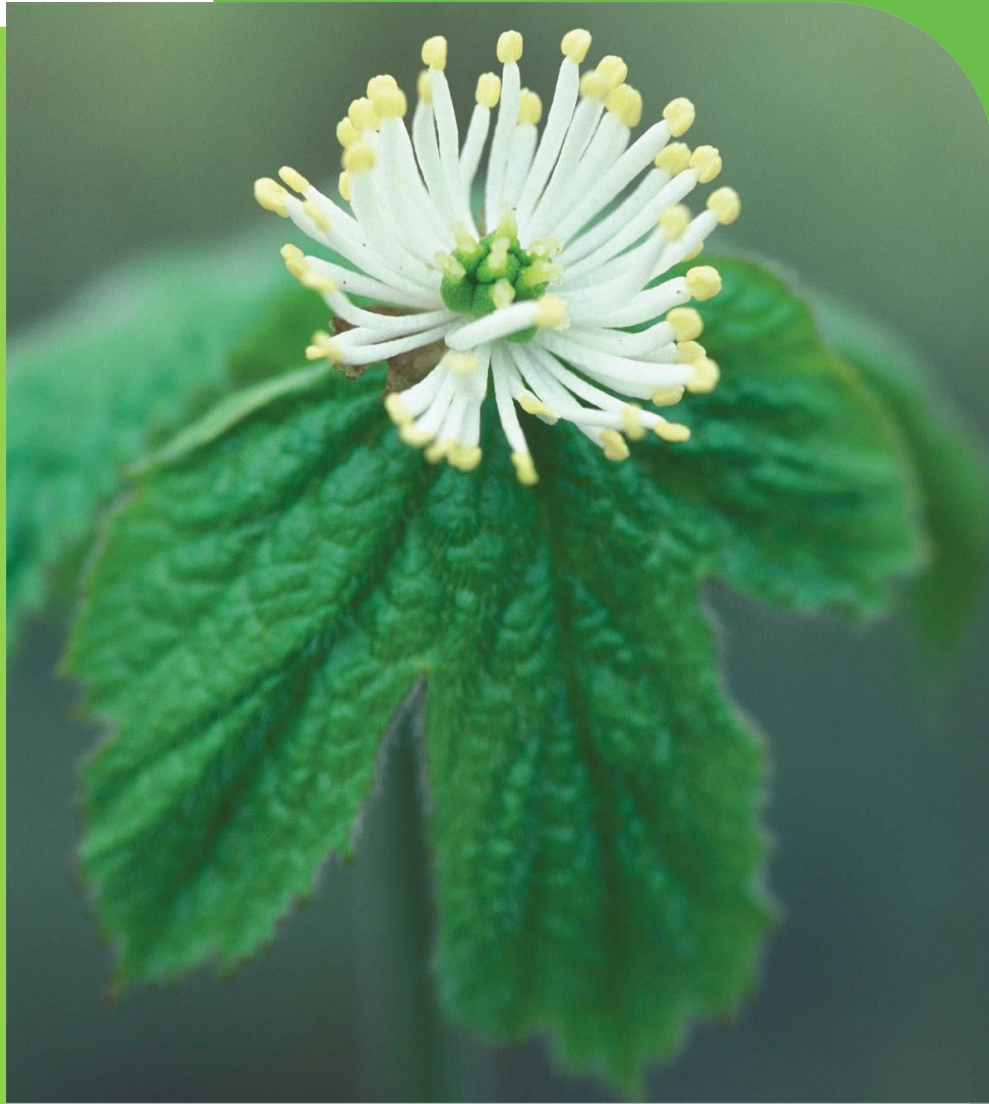
Clinical Evidence for Topical Herbs in Acne

Table 1

Summary of clinical studies evaluating tea tree oil (TTO) products for the treatment of acne.

Treatment group	Trial design	Product application	Efficacy (mean reduction in total lesion count ^a) (%)	Tolerability (frequency of adverse events)	Outcomes
(1) TTO 5% gel (n=58) (2) BP 5% (n=61)	Double-blind ^b	Twice daily (left on) for 8 weeks	(1) 29.3 (2) 45.9	(1) 44% (2) 79%	Both treatments significantly reduced inflamed lesions, although BP better than TTO. Treatments equivalent for reducing non-inflamed lesions and erythema
(1) TTO 5% gel (n=30) (2) Erythromycin 2% gel (n=30)	Investigator-blind	Twice daily (left on) for 6 weeks	(1) 55 (2) 40	Rates not stated; rates for groups not significantly different	TTO significantly better than 2% erythromycin at reducing lesion numbers
(1) TTO 5% gel (n=30) (2) Placebo (n=30)	Double-blind	Twice daily (washed off) for 6 weeks	(1) 43.6 (2) 12.0	(1) 10% (2) 6.7%	TTO significantly better than placebo at reducing lesion numbers. Significant decrease in total lesion count and acne severity index after TTO treatment but not placebo
(1) TTO 5% gel (n=46) (2) TTO 5% gel + Perfect tablet (n=46) (3) Perfect tablet alone (n=48)	Open-label	Gel applied once daily; tablets taken twice daily for 4 weeks	(1) 62.1 (2) 73.7 (3) 73.0	No serious adverse events reported	All treatments significantly reduced lesion number compared with baseline. No statistics performed comparing all groups
(1) TTO 5% extract (n=34) (2) LFCO 5% extract (n=34)	Double-blind	Twice daily for 8 weeks	(1) 38.2 ^c (2) 65.3	(1) 31.3% (2) 12.6%	Inflammatory lesions significantly reduced by both treatments; LFCO better than TTO. LFCO also reduced non-inflammatory lesions

TTO, tea tree oil;
BP, benzoyl peroxide;
LFCO, Lactobacillus fermented
Chamaecyparis obtusa



Traditional Western Herbs and Acne

King's American Dispensatory 1898

Golden Seal (*Hydrastis canadensis*)

- “Acne, seborrhea sicca or oleosa, scrofula, acne rosacea, lupus, sycosis, boils, carbuncles, and ulcers, when dependent upon gastric difficulties, have been greatly benefited and some cases cured by the internal use of the drug alone.”

Calendula (*Calendula officinalis*)

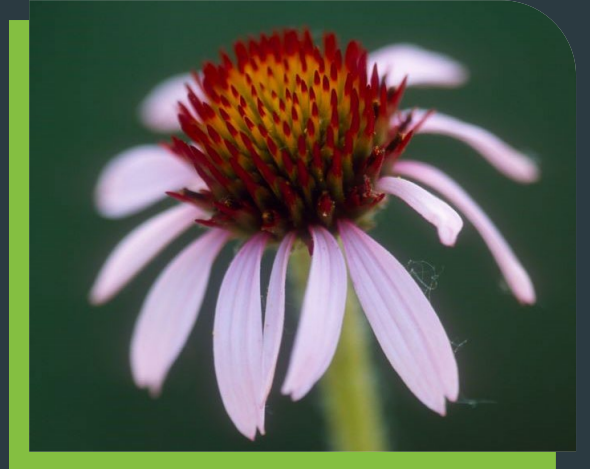
- “Prof. Webster values it in superficial skin affections, even where there are long-standing inflammatory indurations, as in stubborn acne...Use it both locally and internally.”



King's American Dispensatory 1898

Echinacea (*Echinacea angustifolia*)

- “... Dr. Meyer claimed success for this remedy: ...**acne**...and eczema... Subsequent use of the drug has in a measure substantiated the seemingly incredulous claims of its introducer...”



Ellingwood American Mat Med 1919

Oregon Grape (*Berberis aquifolium*)

- “It has cured persistent acne for the writer, when no local treatment was used. It contributes to the removal of **pimples** and roughness and promotes a clear complexion, a soft, smooth and naturally moist skin in sensitive young ladies, when the cause is not a reflex one from ovarian or uterine irritation, or menstrual irregularity.”



Damiana (*Turnera diffusa*)

- “In one most severe case of **acne**, with discoloration of the skin, due to uterine irritation, the results were satisfactory, both to the patient and physician.”





Applying FHT for Acne

Functional Herbal Therapy (FHT)

Goals for Acne Treatment

1. Support key endocrine responses (decrease excess androgens and effects)
2. Eliminate persistent pathogens: *C. acnes*
3. Optimize immune function
4. Eliminate chronic inflammation
5. Address metabolic imbalances (insulin resistance etc)
6. Address gut dysbiosis

Targets from Biomedical Studies

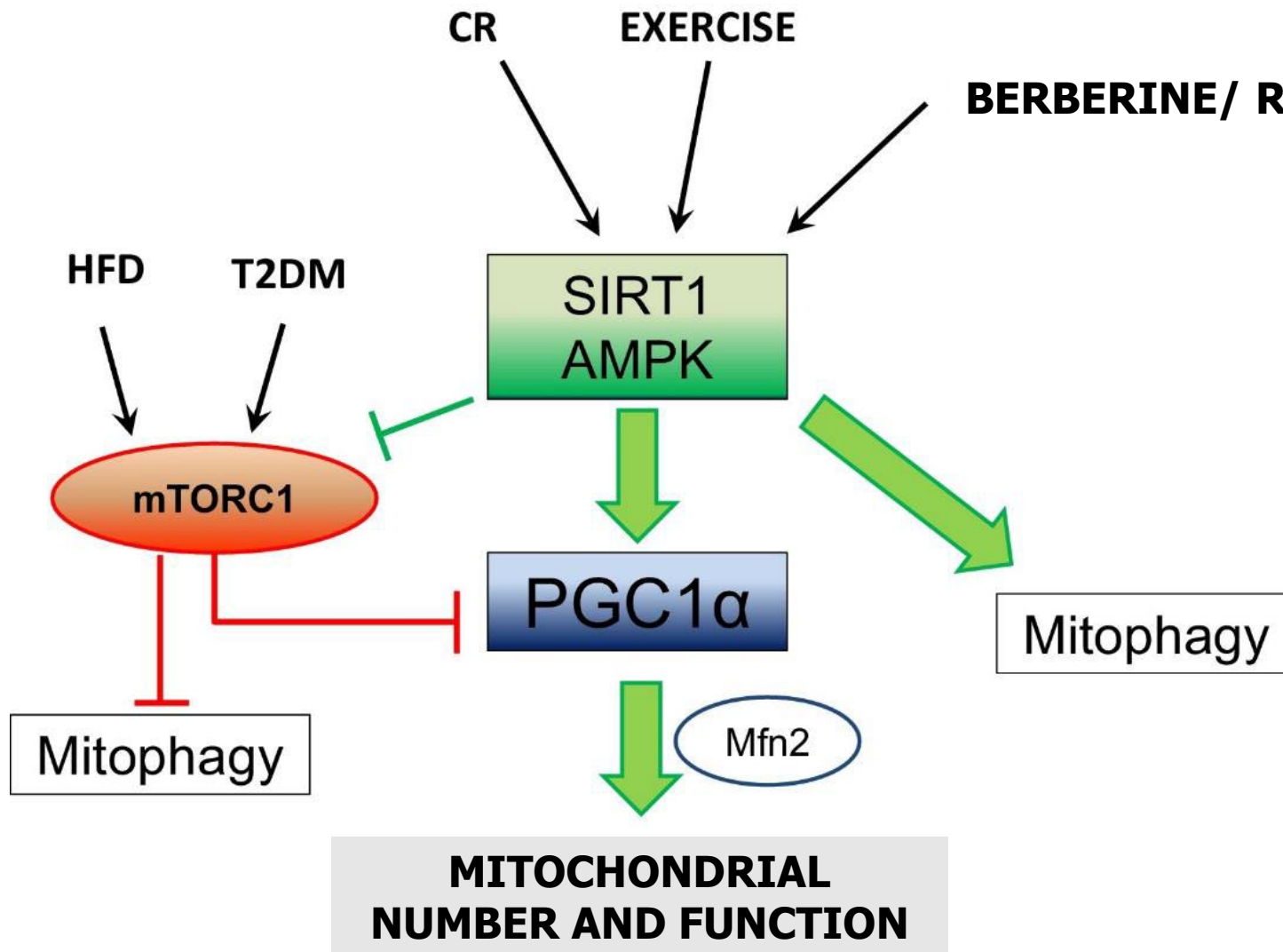
1. mTORC1 = AMPK and SIRT1
2. Insulin, HOMA-IR and IGF-1
3. Androgens, 5-alpha reductase, SHBG
4. Dietary GI and GL
5. Immunity
6. Skin inflammation and microbiome
7. Gut microbiome (emerging evidence)



Table 3. Blood biochemistry values of New York City adults with and without moderate/severe acne

Characteristic	Overall (n = 64)	No acne (n = 32)	Moderate/severe acne (n = 32)	P value
	←—————median (IQR) ^a ————→			
→ Insulin, μ IU/mL ^b	4.0 (2.2-6.8)	3.0 (2.0-4.0)	5.0 (3.0-8.0)	0.002*
→ Sex hormone-binding globulin, nmol/L ^c	52.0 (30.0-93.0)	67.0 (37.0-118.0)	31.5 (25.0-72.3)	0.015*
→ HOMA-IR ^d	0.77 (0.45-1.21)	0.58 (0.37-0.79)	1.04 (0.59-1.65)	0.001*
	←—————mean \pm SD ^e ————→			
→ Glucose, mg/dL ^f	79.3 \pm 6.4	78.4 \pm 6.7	80.3 \pm 6.0	0.243
→ Insulin-like growth factor-1, ng/mL ^{gh}	236.0 \pm 67.1	214.1 \pm 50.7	259.0 \pm 74.9	0.009*
Insulin-like growth factor binding protein-3, mg/L ^{ij}	4.9 \pm 0.7	4.9 \pm 0.8	5.0 \pm 0.7	0.569

^aIQR=interquartile range.



Mfn = mitofusin
 HFD = high fat diet
 T2DM = type 2 diabetes
 SIRT1 = sirtuin 1
 mTORC = metabolic target of rapamycin
 PGC1alpha = peroxisome proliferator-activated receptor gamma coactivator 1-alpha

Berberine and IR in PCOS

	Berberine		Metformin	
	Baseline	After treatment	Baseline	After treatment
Body Composition				
body mass index (kg/m ²)	24.6	22.8	24.0	22.7
waist circumference (cm)	80.0	75.4	81.3	76.9
waist/hip ratio	0.88	0.82	0.90	0.85
Lipids				
total cholesterol (mg/dL)	220	170	224	205
LDL cholesterol (mg/dL)	166	135	162	155
Glucose Metabolism				
fasting blood glucose (mg/dL)	90.0	77.4	91.8	79.2
fasting insulin (mIU/mL)	20.5	10.2	19.9	12.0
HOMA-IR	4.9	2.6	4.7	2.8
Hormones				
total testosterone (ng/dL)	49	35	52	37
free androgen index (%)	6.7	3.2	7.0	3.2
SHBG (nmol/L)	33.7	58.3	34.2	59.5
Table 1. Results of treatment with berberine (1500 mg/day) and metformin in 128 women with PCOS completing the 3-month placebo-controlled trial prior to IVF.				

Hitting the Biomedical Targets

1. Phellodendron, curcumin, Polygonum
2. Phellodendron, Gymnema
3. Chaste tree, St John's Wort, green tea, Phellodendron
4. Gymnema, green tea with meals
5. Echinacea root, Andrographis
6. Curcumin
7. Bowel flora balance protocol



Plus Traditional Herbs

- Golden seal, Oregon grape
- Echinacea root
- Calendula



Some Useful Combinations in Acne

- Andrographis, Echinacea root and Holy Basil
- Cleavers, Sarsaparilla, Oregon Grape, Burdock and Yellow Dock
- Phellodendron, Andrographis, Anise and Oregano essential oils
- Green tea, Turmeric, Grape Seed, Rosemary



Acne Treatment Summary

<i>Clinically Tried Herbs</i>	Green tea, Chaste tree, Milk Thistle, White Peony & Licorice
<i>Traditional Western Herbs</i>	Golden Seal, Calendula, Echinacea, Oregon Grape, Damiana, Poke root, Andrographis, Burdock, Cleavers, Nettle leaf
<i>Nutritional Supplements</i>	Zinc, vitamin D, selenium, Chromium, omega-3 EFAs, lactoferrin
<i>Functional Herbal Therapy</i>	Therapeutic guidelines to address 6 goals (next slide)
<i>Biomedical Targets</i>	Therapeutic guidelines to address 7 goals (next slide)
<i>Topical Treatments</i>	Tea tree oil (5% gel), Poke root ointment, Licorice
<i>Diet</i>	Low in sugar (including fruit sources), GI & GL, saturated fats, BCAAs & animal protein. Dairy free and fiber rich

Acne Treatment Summary

Functional Herbal Therapy Treatment Goals	Therapeutic Guidelines
1. Support key endocrine responses (decrease excess androgens and effects)	Chaste tree, Licorice & White Peony, spearmint tea
2. Eliminate persistent pathogens: <i>C. acnes</i>	Topical applications
3. Optimize immune function	Echinacea, Andrographis
4. Eliminate chronic inflammation	Follow dietary guidelines, probiotics, green tea, bioavailable curcumin
5. Address metabolic imbalances (insulin resistance etc)	Milk Thistle, Phellodendron
6. Address gut dysbiosis	GI flora balance protocol, Golden Seal

Biomedical Targets	Therapeutic Guidelines
1. <i>mTORC1 = AMPK and SIRT1</i>	Phellodendron, curcumin, Polygonum
2. <i>Insulin, HOMA-IR and IGF-1</i>	Phellodendron, Gymnema
3. <i>Androgens, 5-alpha reductase, SHBG</i>	Chaste tree, St John's wort, green tea, Phellodendron
4. <i>Dietary GI and GL</i>	Gymnema, green tea with meals
5. <i>Immunity</i>	Echinacea root, Andrographis
6. <i>Skin inflammation and microbiome</i>	Bioavailable curcumin
7. <i>Gut microbiome</i>	GI flora balance protocol



**Thank you!!
Any questions?**