

Digestive Enzymes for FODMAPs

Helo and we come



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Disclosures

Employee, Stock Options at Kiwi Biosciences (FODZYME)

Today we'll cover

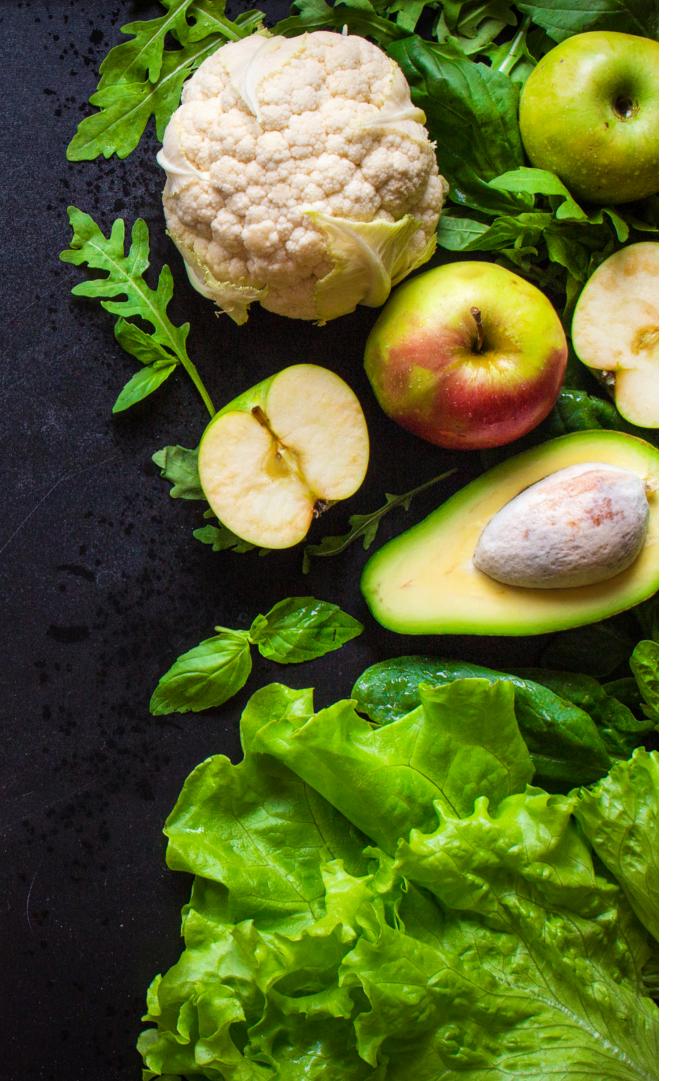
IBS & FODMAP INTOLERANCES DIETARY APPROACHES FOR FODMAPS DIGESTIVE ENZYMES SCIENCE CLINICAL APPLICATION OF ENZYMES

Irritable Bowel Syndrome (IBS) is a Functional GI Disorder

Various mechanisms at play:

- changes in how food moves through the digestive tract
- increased sensitivity to digestion processes (aka visceral hypersensitivity)
- altered immune function and increased inflammation
- altered gut microbiota composition (dysbiosis)





- Fermentable Oligosaccharides Disaccharides Monosaccharides And Polyols
- Short-chain carbohydrates that are indigestible or poorly absorbed by the gut
- Trigger gut symptoms like abdominal pain, constipation, excessive <u>gas</u>, <u>bloating</u>, and diarrhea when they reach the colon
- Symptom onset is generally <u>4-8</u> <u>hours</u> after FODMAP intake



FODMAPs may be troublesome beyond IBS

- Inflammatory GI conditions
- Small intestinal bacterial overgrowth (SIBO)
- Polycystic ovary syndrome (PCOS)
- Endometriosis
- Gastroesophageal reflux disease (GERD)
- Various types of colitis
- Gastric surgeries
- Athletes
- Sub-clinical intolerances

O'Brien L, et.al., 2024.

FODMAPs

and particularly fructan are found in many nutritious and delicious foods and recipes...

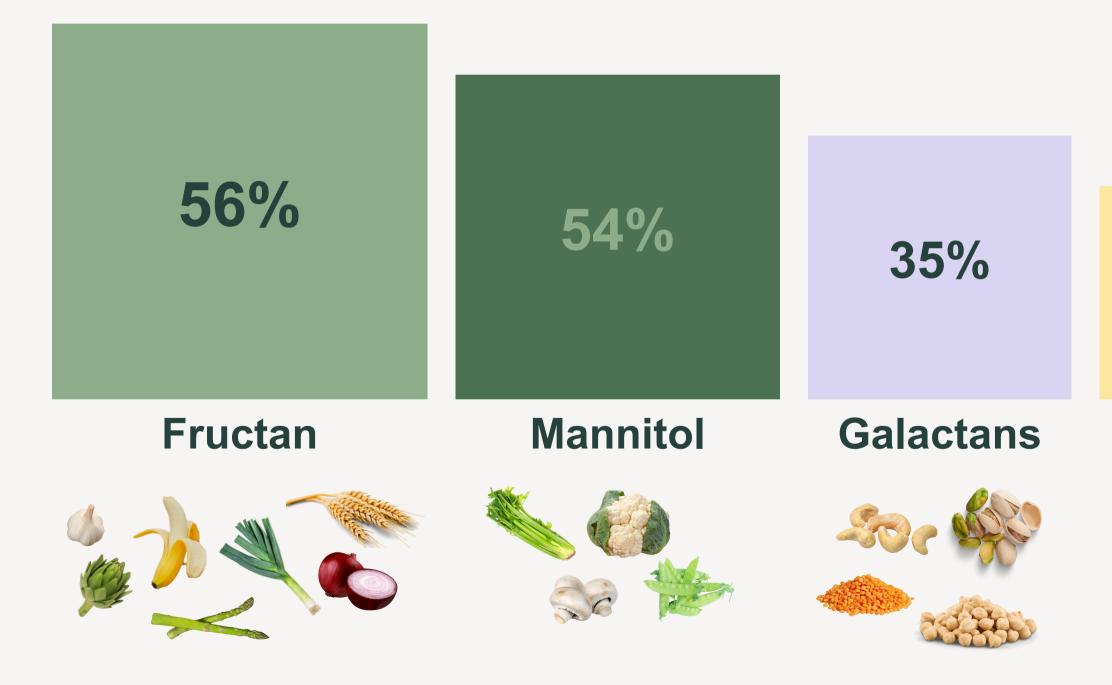
...and are notoriously hard to avoid

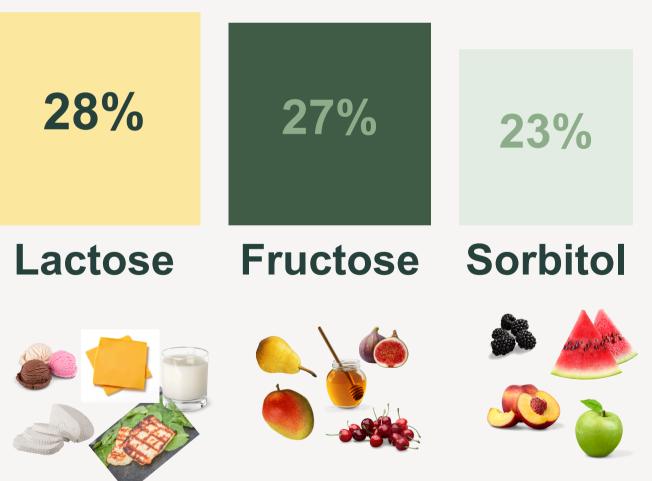
fructan





The most common FODMAP triggers





Van den Houte K, et.al., 2024.



A FODMAP diet is a <u>3 step diet used</u> to help manage the symptoms of IBS.



ELIMINATION

Eliminating / greatly minimizing high FODMAP foods, to assess for symptom relief





REINTRODUCTION / CHALLENGE

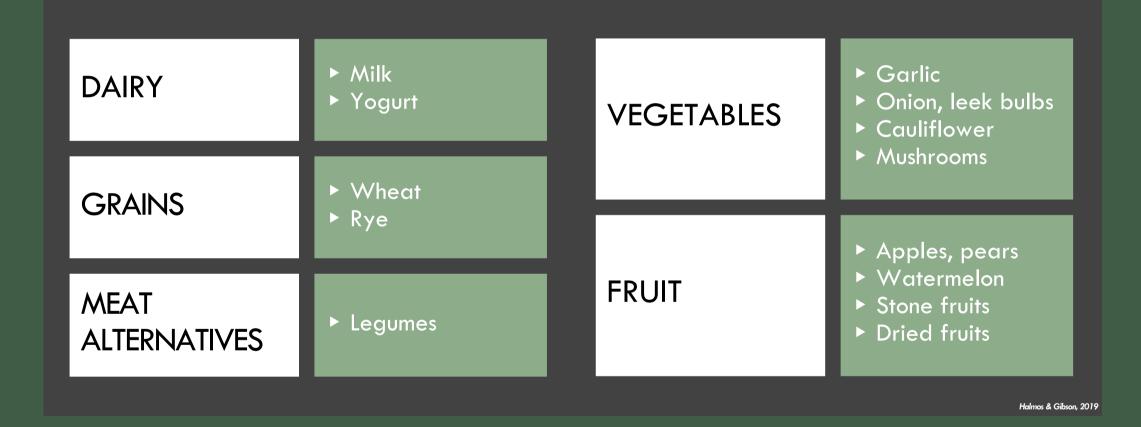
Systematically reintroducing foods containing FODMAPs to learn triggers & tolerance



PERSONALIZATION

Integrating the trigger foods and personalizing their intake

The simplified FODMAP diet



The Simplified FODMAP diet should only be implemented under the guidance of a Registered Dietitian.



TOP DOWN VS. BOTTOM UP

Reduce all FODMAP intake

Monitor response

Challenge each FODMAP group

> ID triggers & refine

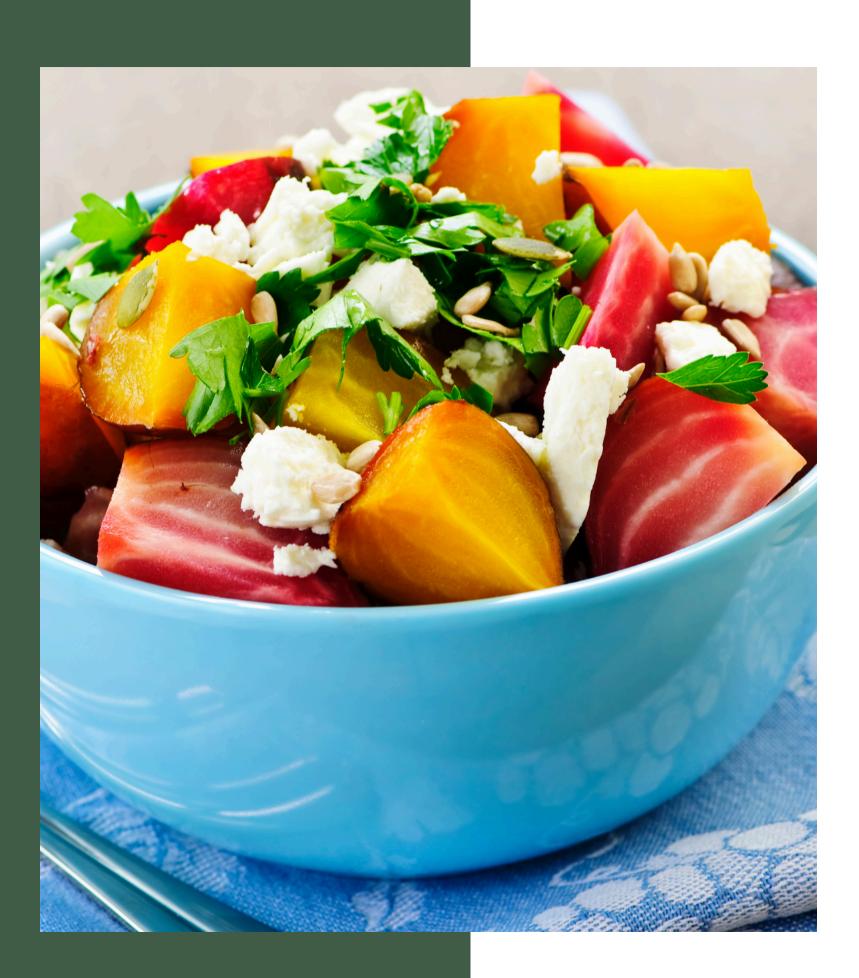
ID triggers & refine

Restrict more FODMAPs as needed (fructose, polyols)

Monitor response

Restrict specific subgroups only Fructan (all, unless limited intake) ► GOS (in those with high intake) Lactose (as triggering)

Singh et. al. 2022



Excessive diet restriction has risks

MICROBIOTA CHANGES

NUTRIENT & ENERGY DEFICIENCIES

SOCIAL ISOLATION AND ANXIETY

FOOD FEARS

INCREASED FOOD COSTS

Staudacher HM, 2017.

SUPPLEMENT VS. DIET INTERVENTIONS

Advantages

Good adherence (convenience, simplicity and ease of administration) Little interference on daily life Low dietary impact (limited impact on usual diet, foods, and nutrients) Ease of understanding (limited education from clinician required) High precision (exact dose and composition can be advised and consumed) **Disadvantages**

Medicalization (and recall required for adherence)

Cost and availability

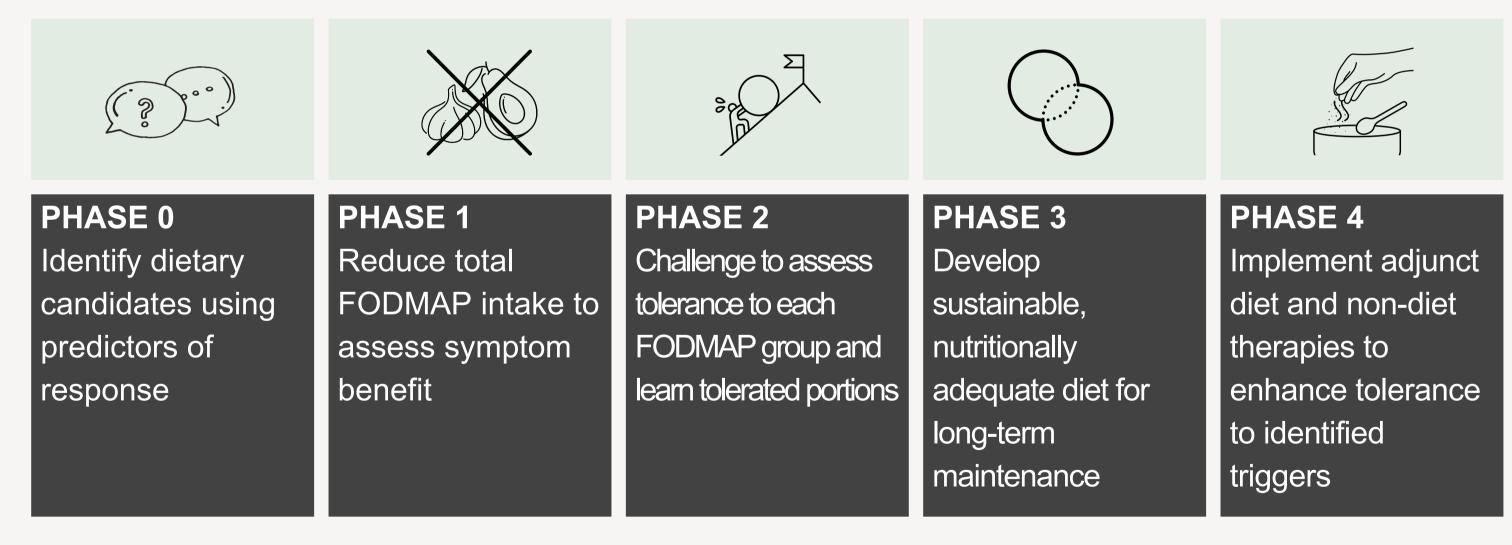
Supplements powders, capsules, etc.

Advantages Low medicalization (perceived as natural and self-managed) Personalizable & broadly applicable Disadvantages Variable adherence High impact on daily life Cost and availability High dietary impact **Requires understanding and education** Low precision due to differences in clinician delivery and patient adherence

Diet Interventions Change in quantity or type of foods Whelan K, 2024.

Proposed 5-phase FODMAP framework

This updated approach includes a new Phase 0 to identify ideal candidates for FODMAP approaches based on predicted response and Phase 4 to implement adjunct diet and non-diet therapies



O'Brien L. et. al., 2024.

Adapting the FODMAP diet in IBS —

Ideal candidates and key considerations

Ideal IBS candidates Traditional three-phase FODMAP approach Patients who • Curr		
	 Lack of identifiable patterns for symptom generation with food 38 	• More restrictiv
	 Have sufficient motivation and resources to conduct the diet in full 	approach, but
		term success o
FODMAP-gentle approach	Patients who are	• Dietetic assess
	 Eating large concentrations of FODMAPs 	• Robust trial ev
	 Mildly symptomatic 	• Traditional IBS
	• Children	evidence of eff
	• Elderly	
	 Nutritionally compromised 	
	 Following other dietary restrictions 	
	 At poor capacity to understand and/or apply the diet 	
	 Preferred to follow this approach 	
Low-FODMAP Mediterranean diet	 Psychological symptoms (anxiety/depression) 	• Time to prepar
	 Cardiovascular risk factors 	• Adequate finar
	 Patients with poor-quality diets 	• Access to Medi

Key considerations

- ence best supports this approach
- ivered education superior to booklet-delivered education 39
- tive dietary adjustments required at outset as compared to FODMAP-gentle
- It may be better able to identify specific food triggers and hence improve longto of the diet $\frac{40}{2}$
- ssment of habitual diet will guide the choice of diet application
- evidence for the FODMAP-gentle diet is lacking
- BS dietary advice shares features of a FODMAP-gentle diet, with some
- efficacy for symptom management

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Additional contraindications for full LFD

 History of or current disorded eating At risk for disordered eating • Picky eaters No IBS diagnosis

DIGESTIVE ENZYME SCIENCE



What are digestive enzymes?

Enzymes are highly specialized proteins (chains of amino acids) folded in particular ways. Digestive enzymes can act on troublesome foods, including FODMAPs, to break them down.

ENZYMES CAN TARGET MANY TYPES OF CARBOHYDRATES

	SUBSTRATE	ACTIVE ENZYME
	Fructan (inulin, FOS, levan)	Fructan hydrolase
	Fructose	Glucose/xylose isomerase
	Galactooligo-saccharides (GOS)	Alpha-galactosidase
	Inulin	Inulinase (Endo or Exo)
	Lactose	Lactase
	Polyols (mannitol, sorbitol)	Under development
	Pectin	Pectinase
	Sucrose	Sucrase
	Starch	Amylase & glucoamylase
	Insoluble fiber	Hemicellulase





Enzymes for FODMAPs

Targeted use of digestive enzymes with FODMAP-containing foods helps break down their FODMAP content before they can trigger symptoms.

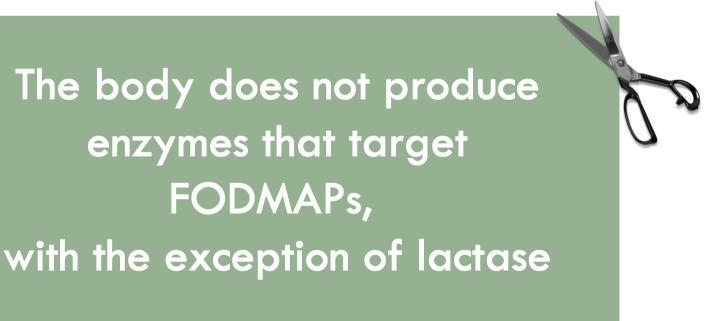
Digestive enzymes act as specialized <u>molecular scissors</u> to molecules, making them easier to digest.

ENZYMES FOR VARIOUS FODMAP FAMILIES:

- Lactase
- Alpha-galactosidase
- Fructan hydrolase
- Glucose/xylose isomerase*



break down FODMAP





Clinical guidelines on enzymes

Guidelines in peer-reviewed journals and by Monash University on how to implement the low FODMAP diet recommend the use of digestive enzymes to enable:



Management of symptoms, eg. bloating, gas, diarrhea, constipation



Dietary flexibility and reduced anxiety around social or uncontrolled food environments



Long-term sustainability and expanded food options to meet nutrition needs

Safety and efficacy of enzymes

Research shows that patients with FODMAP sensitivities benefit from using enzymes with otherwise triggering foods:



Supplemental lactase reduces bloating, abdominal pain and gas in both adults and children



In those with IBS, alpha-galactosidase prevents bloating and gas and reduces global distress following galactan-rich meals



Multi-enzyme blends show promise in controlling overall symptoms, and for individual symptoms like bloating, gas and abdominal pain





Candidate profiles

A variety of patients can benefit from use of digestive enzymes

	Ideal IBS candidates	
Traditional three-phase FODMAP appro	oach Patients who	• Current eviden
	Have more severe symptoms	• Dietitian-delive
	• Lack of identifiable patterns for symptom generation with food $\frac{38}{38}$	More restrictive
	 Have sufficient motivation and resources to conduct the diet in full 	approach, but
		term success of
FODMAP-gentle approach	Patients who are	• Dietetic assess
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	 Nutritionally compromised 	
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Digestive enzymes can be a first-line intervention in those:

Already on a highly restrictive diet

With disorded eating or at risk

Lacking access to low FODMAP foods

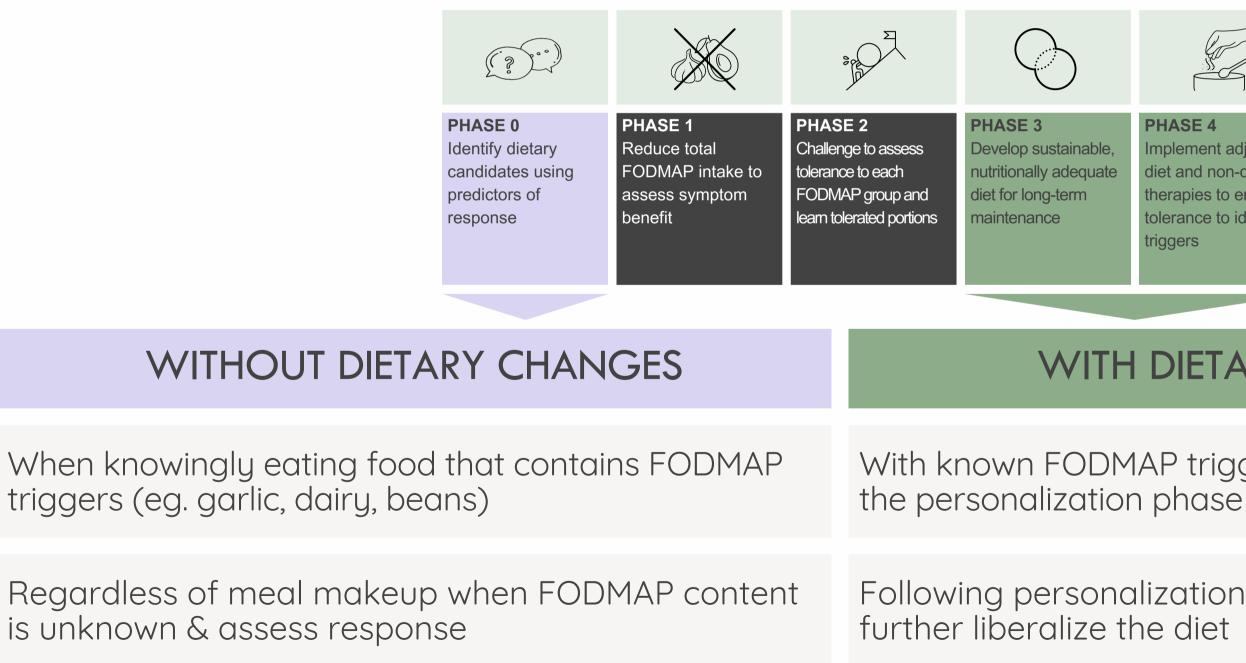
With poor compliance to diet recommendations

Who are elderly or at risk for malnutrition

Digestive enzymes help liberalize the diet of anyone with sensitivities to the FODMAP that the enzyme targets

Ways to use digestive enzymes Enzymes may be used with or without dietary change based on a patient's indications and

awareness of FODMAP triggers





PHASE 4 Implement adjunct diet and non-diet therapies to enhance tolerance to identified triggers

WITH DIETARY CHANGES

With known FODMAP triggers during

Following personalization phase to

Intolerances guide enzyme selection

Patients with multiple FODMAP intolerances benefit from combination products

LACTOSE	Milk, ice cream, frozen yogurt, gelato, soft ch
Lactase	etc), yogurt, kefir, pudding, custard, condens
FRUCTAN	Onions, garlic, scallion, shallot, leek, wheat, b
Fructan hydrolase	artichoke, grapefruit, Brussels sprouts, dried
GALACTANS	Beans, beets, lentils, chickpeas, falafel, hum
Alpha galactosidase	tofu, peas, cashews, pistachios, kale, taro, to
FRUCTOSE	Apples, pear, fig, mango, watermelon, fruit j
Xylose/glucose isomerase	nectar, high fructose corn syrup, candies ar

selection m combination products

cheeses (ricotta, cottage, paneer, ised milk

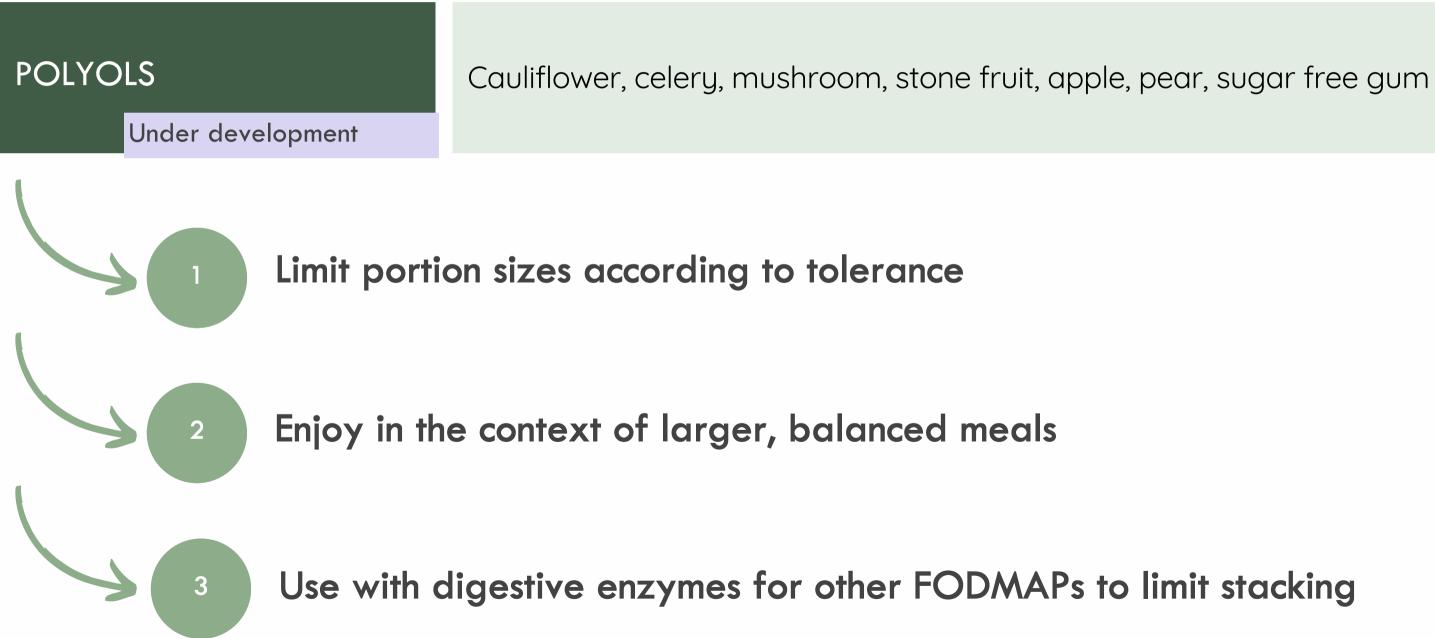
oarley, rye, spelt, inulin, FOS, d fruit, beets, Savoy cabbage

nmus, soymilk, soybeans, soft tomatillo, almond meal

juice/smoothies, honey, agave Ind sweets, sugar snaps

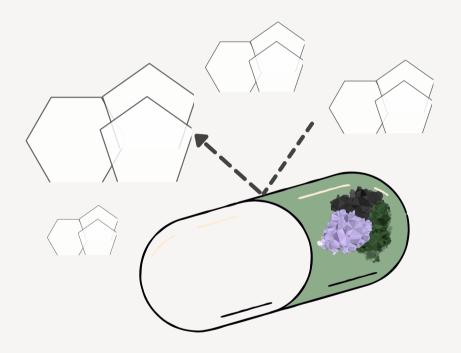
A note on polyols

Tips to support tolerance



Powders vs. Capsules

A powder facilitates optimal contact between enzymes and FODMAPs for maximum FODMAP break down





ENZYMES IN CAPSULES:

- isolated from FODMAP substances
- deactivate in the stomach
- are digested themselves

ENZYMES IN POWDER FORM:

- integrate easily with FODMAPs
- distribute freely in food in the gut

• get to FODMAPs faster & break them down

So D. et. al. 2024.

What to look for in an enzyme How to choose an effective digestive enzyme for patients

TARGETED Designed for known or suspected triggers. Beware of generic "enzyme blends" FORMULA that do not contain evidence-based enzymes or not at therapeutic levels MODE OF A powder form maximizes an enzymes' effect, while capsules reduce their ability **ADMINISTRATION** to homogenize with and break FODMAPs down NO OTHER Avoid supplements formulated with mannitol, sorbitol, lactose, carrageenan, GUT TRIGGERS artificial sweeteners and other gut irritants BACKED BY Be cautious when non-peer reviewed or 'marketing' studies are cited. RESEARCH Also be wary of claims solely on background bioactives research



Benefits of regular use

Support better digestion of trigger foods by reducing overall FODMAP load and stacking

Reduce food fears and anxiety to facilitate greater confidence with food and social eating



Increase flexibility to have a more varied, nutrient-rich and diverse diet

Specific nutritional benefits



NUTRITIONAL DIVERSITY

Avoid nutrient deficiencies and promote health (eg. calcium-rich dairy to support bone health)



PLANT-BASED FIBER FOODS

Increase fiber variety and tolerated volume to support microbiome health



PROTEIN BEYOND MEAT

Increase high-FODMAP protein foods like tofu, peas, legumes, nuts, soy and dairy





Getting patients started

TRIGGERS

FODMAP FOOD

3

USE AS FREQUENTLY AS NEEDED

APPLY TO KNOWN OR SUSPECTED FODMAP

ADD TO FIRST BITE OR DURING START OF MEAL

EXPECT BENEFIT 4-8 HOURS AFTER HIGH



Troubleshooting

FIBER	increa fiber r
HYDRATION	encour especi
PORTION SIZES	listen t mindfu
OTHER TRIGGERS	monito caffeir

use gradually, diversify types, consider manipulation (eg. hummus vs. chickpeas)

rage hydration throughout the day, ially as fiber intake increases

to satiety cues, eat slowly and ully, chew well

or fatty and spicy foods, alcohol, ine, carbonation and artificial sugars

Supporting behavior change



EDUCATE ON LINK BETWEEN GI DIET AND FOOD ANXIETY History of a restrictive diet, such as low FODMAP or gluten-free, is associated with 3x more risk for disordered eating behaviors



DISCUSS SIGNS OF EXCESSIVE RESTRICTION

Avoidance of food due to fear of symptoms or difficulty socializing due to restrictions can point toward the need for expansion



EXPLORE RELATIONSHIP WITH FOOD

How would you describe your relationship with food? Do you feel anxious around food? Do you skip meals due to fear of GI issues?





Communication tips & common questions

Does this mean I can eat anything I want now?

How do I know what has FODMAPs in it?

Can I cook with digestive enzymes?

Will I become dependent on enzymes?

How much do enzymes cost?



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Common multi-FODMAP meals

AMERICAN	MEDITERRANEAN	SPANISH	MEXICAN	JAPANESE	ITALIAN
Meatloaf with onion gravy	Falafel in pita with tzatziki	Chorizo with onion & pepper on wheat bun	Quesadilla with flour tortilla & poblano	Udon with silken tofu	Artichoke pizza
Cheeseburger with onions	Couscous with chickpeas & currants	Paella with peas, artichoke & asparagus	Nachos with cheese & scallions	Pumpkin curry with scallions	Penne alla vodka
Parfait with cranberry granola	Pomegranate fattoush	Gazpacho with croutons	(scallion		Vegetable Iasagna
Smoothie with banana, spinach & regular milk	Halloumi kebabs with onion & zucchini	Pan con tomate	Tacos with jicama slaw on flour tortilla	Sukiyaki with savoy cabbage	Pistachio gelato

There is no cure for Functional GI Disorders







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Thank you!

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