Fullscript

Dietary supplements

A CLINICAL GUIDE FOR PRACTITIONERS



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At Fullscript, we believe that dietary supplements are core to an integrative treatment plan.

From nutraceuticals to botanicals to multi-ingredient formulations, there's no shortage of options for practitioners interested in recommending supplements, and the industry continues to innovate at an incredible pace. With thousands of products available through Fullscript, it's sometimes difficult to know where to start.

As healthcare practitioners, it's critical that we remain well-informed about all the options available to us so that we can best support our patients.

We hope this booklet provides you with the initial information needed to comfortably use dietary supplements in your practice. Our world-class customer success team is always available to answer questions, or connect you with our integrative medical advisory team for guidance on product selection and protocol development.

In health,

Dr. Alex Keller, ND Medical Director Fullscript



Supplements 101

Regardless of your experience level, the supplement landscape can easily become overwhelming. This section will touch on some key categories of supplements and how to best work with them.

Supplements can be divided into three key categories:



Nutrients

also known as Nutraceuticals or Orthomolecular Medicine



Botanicals

also known as Herbal Medicine or Phytotherapy



Hormones

also known as Hormone Replacement Therapy or Restorative Medicine

Each category is meant to support underlying excesses or deficiencies, with the ultimate goal of bringing the body back into balance. Where it can become complicated is in understanding the different uses and dosing of specific extracts, chelates, preparations, and more. In the Fullscript catalog alone, there are over 20,000 unique products to filter through and understand.

Let's try to make some sense of it all...

Nutrients



For the purpose of this guide, nutrients are defined as ingredients that would otherwise be found in food including vitamins, minerals, phytochemicals and antioxidants.

What are nutrients?

In order to sustain life and wellness, the human body requires a careful balance of a broad range of nutrients, categorized as macronutrients and micronutrients.

Macronutrients constitute the major food groups of carbohydrates, fats and proteins. They are required in large amounts, used primarily for energy production and tissue growth.

Micronutrients are required in trace amounts and include vitamins and minerals. Phytonutrients, such as anthocyanin found in blueberries or resveratrol found in grapes, are also often classified as micronutrients.

How do nutrients work?

Macronutrients are the caloric basis for our daily energy need, but also provide the building blocks of tissue development, fiber for our microbiota, cholesterol for hormone production, and more.

Micronutrients are not relevant for energy and instead contribute to tissue development, hormone and neurotransmitter production, brain function, immune function, and more. For a detailed review of the key dietary nutrients, visit **www.fullscript.com/hcp**

Common examples of nutritional supplements

Dietary supplements can provide a wide array of nutrients in condensed form, allowing users to target specific deficiencies or upregulate certain pathways that require those nutrients in abundance.

Some common examples include:

- Whey protein isolate
- Omega 3 fatty acids
- Calcium
- B vitamins



Botanicals



For the purpose of this guide, botanicals are defined as therapeutic plant extracts, not otherwise intended as food, including whole plant extracts and specific phytochemical extracts.

What are botanicals?

Considered the original pharmacy, records of humanity using botanical extracts therapeutically date back to the beginning of recorded history. More recently, botanical medicine has served as the inspiration for numerous pharmaceutical inventions and continues to reveal its purposes via modern research.

For the integrative practitioner, botanical medicine is essential, normally eliciting far fewer and less significant adverse effects than pharmaceutical interventions. A growing body of research shows that if used in correct dosages, certain botanical extracts are in fact more effective than pharmaceutical equivalents, and often more cost effective as well.

How do botanicals work?

Botanical medicine has as broad a pharmacopeia as modern pharmaceuticals. Given their capacity to interact with virtually every bodily system and tissue, there are literally thousands of therapeutic uses for botanicals. Although there is a vast amount of literature on the traditional use of botanical medicine, there is only a scant amount of modern research relative to modern pharmaceutical interventions. As a result, it becomes somewhat challenging to compare most botanicals with pharmaceuticals regarding clinical outcomes. However, according to a recent World Health Organization report, this landscape is rapidly evolving.

For a review of the various uses and existing clinical research supporting botanical medicine, visit **www.fullscript.com/hcp**.

Examples of botanical ingredients

Botanical medicine can provide an abundance of therapeutic effects, allowing everyone, from the skilled practitioner to the common layperson, to apply these therapies effectively.

Some common examples include:

- Garlic (Allium sativum) immune function, cardiovascular function
- **Berberine** lowering blood sugar, decreasing triglycerides, antimicrobial
- **Reishi –** immune function, potential anti-cancer properties

Note: The form of extract is very important in botanical medicine. Plants contain a variety of therapeutic chemicals, differing in their use and extraction process. Practitioners should not only understand the existing clinical research and how to dose these extracts for therapeutic purposes, but also to prevent harm.

Hormones



In integrative medicine, hormone therapy typically involves the use of bio-identical versions of plant extracts, mimicking the chemical structure of endogenously produced hormones.

What are hormones?

Hormones are chemical messengers produced by the endocrine glands. These messengers have an effect on most tissues and major bodily functions. Establishing and resolving the causes of hormonal imbalance is one of the core therapeutic systems applied not only in integrative medicine, but in conventional medicine as well.

How do hormones work?

Hormones are abundant in the body's circulation, but cells require specific receptors for hormones to elicit an effect. When a hormone binds to a specific receptor, it causes a biological response within that cell, which is why a singular type of hormone can have such a broad effect. The entire endocrine system is based on positive and negative feedback loops, which inform endocrine glands whether more or less hormones should be produced.

While balance of endogenous hormone production is ideally maintained via diet and lifestyle, disease can easily occur when this delicate balance is disrupted. If this happens, exogenous hormones can be used to elicit similar or identical effects on the same cell receptors. However, considering their broad and potent effect on a variety of systems, using hormones therapeutically must be done with caution and skill. Longterm adverse effects are not uncommon with hormone therapy, and its use should be limited to highly-trained practitioners.

Examples of hormone ingredients

Exogenous hormones are available in a variety of forms. It should be noted that certain nutrients may also be supplemented to upregulate the endogenous production of hormones.

Some common examples include:

- **Pregnenolone** the 'mother' of the steroidogenic hormone pathway
- Dehydroepiandrosterone (DHEA) –
 elevates estrogen and testosterone
- Vitamin D regulates bone density, balancing parathyroid hormone secretion

Preliminary evidence demonstrates broad and highly beneficial therapeutic uses for exogenous hormones. However, similar to botanical medicine, hormone therapy should be used exclusively and with caution by skilled clinicians.

How to read a supplement label

Sur	opl	em	ent	Fac	cts	•
Ju	JU	CIII	CIII	L C C	-13	•

Serving Size 2 Capsules Servings Per Container 30

	~	
	Amount Per Serving	% Daily Value
	, i i i i i i i i i i i i i i i i i i i	
Vitamin C	500mg	834%* 🔶
Zinc	20mg	199%*
Beta Glucans	300mg	t 🔶
Echinachea purpurea	100mg	<u>†</u>
Standardized to 4% alkylamides (4 mg)		
Proprietary blend	500mg	
Echinacea angustifolia (leaf)		†
Allium sativum (bulb)		†
Withania somnifera (root)		t
Ganoderma lucidum (aerial parts)		†
Rhodiola rosea (root)		†
Andrographis paniculata (aerial parts))	†
* Percent Daily Values are based on a 2,000 † Daily Value not established	calorie diet.	

The "Supplement Facts" title is an indicator that the product is marketed for sale in the U.S. and is an FDA standard.

The serving size, and sometimes the number of servings per container, will be included to help you compare more easily between products.

 Make sure the serving sizes match when comparing supplements to get an accurate comparison between the products.

Vitamins and minerals will always show the dose in both weight and % daily value to help you understand how you're hitting your dietary requirements.

- Many supplements will have doses that exceed the recommended daily value.
- Dietary supplement ingredients that are not vitamins or minerals will not have a % daily value as they are not essential ingredients in the diet.

Dietary supplements are regulated by the FDA, and all labels must follow a consistent format to make it easier for consumers to understand supplements. There are some tricks to understanding dietary supplement labels well, so be sure to pay attention to the following points when you're evaluating your supplements.

Supplement Facts

Serving Size 2 Capsules Servings Per Container 30

	Amount Per Serving	% Daily Value	
Vitamin C	500mg	834%*	
Zinc	20mg	199%*	
Beta Glucans	300mg	t	
Echinachea purpurea	100mg 🔴	1	
Standardized to 4% alkylamides (4 ma)	•	_	
, , , , ,		_	
Proprietary blend	500mg 🔵		
Echinacea angustifolia (leaf)		t	
Allium sativum (bulb)		+	
Withania somnifera (root)		†	
Ganoderma lucidum (aerial parts)		t	
Rhodiola rosea (root)		†	
Andrographis paniculata (aerial part	s)	t	
* Percent Daily Values are based on a 2,000	0 calorie diet.	-	

Herbs will sometimes have additional information listed in the supplement facts panel. You might see ratio numbers (i.e. 4:1) that designate how much raw material of the herb (fresh or dried herb) went into making the supplement version of the herb.

Herbs might have a standardization amount that corresponds to how much of an active ingredient is present in the herbal supplement. The dose of the active ingredient is often listed, but not always.

Proprietary blends are common in dietary supplements. Only the total amount of the proprietary blend in a serving needs to be listed on a supplement, which means that you don't get all of the information about every ingredient that is in the blend.

Ingredients in a proprietary blend are listed in order from most to least. This is similar to how food ingredients are listed on nutrition facts panels that you find on prepared foods.

The daily value percent is established against a 2,000 calorie diet. While this is the standard calorie amount across most labels, it's always important to scale your requirements based on the calorie intake that you need to reach your health goals. Developing individualized treatment plans that combine pharmaceuticals with supplements can easily become complicated. The following charts allow for quick referral when working with the most common pharmaceuticals.

The information provided in the following charts is based on a review of literature available at the time of publication. While the content is considered to be accurate at the time of publication, new or updated research released after the publication date may impact the accuracy of the information. Please use clinical discretion when consulting this resource and refer to the online resources* for the most recent versions.

Drug-nutrient interactions

Pharmaceutical	Class of drug	Nutrient	Interaction	Class
Acetaminophen/	Pain Narcotic, Anti-Inflammatory	Caffeine	Increases analgesic effects	А
Hydrocodone			Increases absorption	В
vicouit, Norco			Increases elimination of drug	С
		Alcohol	Increases risk of hepatotoxicity	В
			Induces CYP2E1	С
Albuterol Ventolin, Proventil	Breathing Bronchodilator	None	No significant interactions confirmed	N/A
Amlopidine Norvasc	Blood Pressure Calcium Channel Blocker	Grapefruit Juice	Inhibits CYP3A4; slightly increases plasma concentration of drug	С
Atorvastatin	Cholesterol	Grapefruit Juice	Increases serum atorvastatin;	В
Lipitor	Statin		Induces CYP3A4; increases plasma concentration of atorvastatin acid and atorvastatin lactone	С
		St. John's Wort	Increases LDL and total cholesterol	С
Gabapentin Neurontin, Neuraptine	Neuropathy, Pain	Alcohol	Gabapentin is safe to use in treatment of alcohol dependency; reduces symptoms of alcohol withdrawal	A
		Cannabis	Gabapentin reduces symptoms of cannabis withdrawal	В
Insulin Glargine Injection	e Diabetes Insulin analogue	None	Potentially significant theoretical interaction	F
Lantus Solostar			See the white paper for further details	

* Note: For more information on the Fullscript research process and classes of evidence, see the full white paper at: www.fullscript.com/hcp.

Pharmaceutical	Class of drug	Nutrient	Interaction	Class
Levothyroxine Levothroid, Synthroid	Thyroid Synthetic Thyroxine	Calcium	Decreases absorption of drug; increases TSH	В
		Vitamin C	Increases absorption of drug; decreases TSH	В
		Coffee	Decreases absorption of drug	С
		Grapefruit Juice	Inhibits OATP1A2; slightly decreases absorption of drug	С
Lisinopril Prinivil, Zestril	Blood Pressure ACE Inhibitor	None	No significant interactions confirmed	N/A
Metformin Glucophage XL,	Diabetes (biguanide)	Berberine (300 mg)	Improves insulin sensitivity; decreases HOMA-IR, total cholesterol, LDL	В
Gluformin	Hepatic Glucose Reducer	Alcohol (>7 drinks/week)	Increases effect of drug; increases lactic acidosis and lactate production	С
Metoprolol Lopressor, Toprol-XL	Blood Pressure Beta-blocker	None	No significant interactions confirmed	N/A
Omeprazole Prilosec, Zegerid	Acid-Reflux Proton Pump	St. John's Wort	Induces CYP2C19 and CYP3A4; decreases effectiveness of drug	С
	Inhibitor	Grapefruit Juice	Inhibits CYP3A4; inhibits metabolism of drug	С
Rosuvastatin Crestor	Cholesterol Statin	Grapefruit Juice	Inhibits OATP2B1; reduces bioavailability of drug	С
		EGCG	Significantly reduces systemic exposure of drug	С

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Drug-nutrient depletions

Pharmaceutical	Class of drug	Nutrients depleted	Recommended dosage	Class
Acetaminophen/	Pain	Glutathione	NAC - FDA approved protocol	В
Hydrocodone Vicodin, Norco	Narcotic, Anti-Inflammatory		Loading phase: 0.14 to 0.16 g/kg up to 17 doses.	
			Maintenance: 0.069 to 0.083 g/kg	
Albuterol Ventolin, Proventil	Breathing Bronchodilator	No significant depletions confirmed. See white paper for details.	N/A	N/A
Amlopidine Norvasc	Blood Pressure Calcium Channel Blocker	No significant depletions confirmed	N/A	N/A
Atorvastatin Lipitor	Cholesterol Statin	Coenzyme Q10	50-200 mg/day	В
Gabapentin Neurontin, Neuraptine	Neuropathy, Pain	Folic Acid	400 mcg/day	В
Insulin Glargine Injection Lantus Solostar	Diabetes Insulin analogue	Magnesium	336 mg/day for 3 months	В
Levothyroxine Levothroid, Synthroid	Thyroid Synthetic Thyroxine	No significant depletions confirmed	N/A	N/A
Lisinopril Prinivil, Zestril	Blood Pressure ACE Inhibitor	Zinc	11 mg/day for men and 8 mg/day for women	А
Metformin	Diabetes	Vitamin B12	1000 mcg/day sublingual	В
Glucophage XL, Gluformin	(biguanide) Hepatic Glucose Reducer	Folic Acid	5 mg/day	В
Metoprolol Lopressor, Toprol-XL	Blood Pressure Beta-blocker	No significant depletions confirmed. See white paper for details.	N/A	N/A
Omeprazole	Acid-Reflux Proton Pump Inhibitor	Magnesium	250-300 mg/day	А
Prilosec, Zegerid		Vitamin B12	1000-2000 mcg/day	С
		Calcium	500-1000 mg elemental calcium (carbonate, citrate) 3x/day	С
		Iron	105–210 mg/day elemental iron	С
Rosuvastatin Crestor	Cholesterol Statin	Coenzyme Q10	50-200 mg/day	А



Determining supplement quality

Working with high-quality dietary supplements is crucial for clinical outcomes. But what does high-quality even mean?

There are a few key factors to assess when selecting the products you work with:

- Ingredient sourcing
- Ingredient absorption
- Product manufacturing

Ingredient sourcing and absorption

The source of ingredients when working with both simple and complex patient cases is the first step in determining whether you will have a high-quality end product. If working with nutrients, one might question whether the ingredient is naturally derived or synthetically produced. If the latter, this will have an effect on absorption and/or cause side effects.

For the purpose of this introductory resource, let's consider iron. There are various forms of iron found in dietary supplements. Three examples include:

- Ferrous fumarate
- Ferrous bisglycinate
- Heme iron

Ferrous fumarate is the iron salt from fumaric acid, which is found naturally in certain mushrooms and moss species, but is typically synthetically manufactured from malic acid in apples.^{4,5} Ferrous fumarate is one of the most common iron-based ingredients in dietary supplements due to its affordability, but it is also often shown to be associated with constipation.⁶

Ferrous bisglycinate is an iron chelate, meaning it is manufactured to bind one molecule of ferrous iron to two molecules of the amino acid glycine. The patented version of ferrous bisglycinate is known as Ferrochel.⁷ Iron bisglycinate is widely thought to be more absorptive than ferrous fumarate, therefore, causes less constipation.⁸ Iron chelates normally price in the mid-range of iron ingredients.

Heme iron is derived mainly from hemoglobin and myoglobin in animal tissue. It is absorbed more efficiently than nonheme iron, at a rate of 15% - 35%, depending on the person's current iron saturation levels. Heme iron, although typically the most expensive form of supplementary iron and not vegan-friendly, is considered the best absorbed form of iron.⁹



Similar examples exist for most supplement ingredients, so please take the time to review the ingredient summaries at **www.fullscript.com/hcp** to learn more about the wide variety of options available.

Product manufacturing

Supplement product manufacturing standards vary widely in the United States. However, as of 2007, all United States supplement manufacturers are required to comply with FDA-mandated Current Good Manufacturing Practice (CGMP) guidelines. Typically, CGMP standards are considered the baseline to "ensure the quality of the dietary supplement and to ensure that the dietary supplement is packaged and labeled as specified in the master manufacturing record."¹⁰

Beyond CGMP, many supplement manufacturers will elect to apply voluntary third-party certification to their manufacturing or ingredient-sourcing standards.

See the chart on the next page for some common examples of third-party certifications.

At Fullscript, we believe quality is uniquely defined by each individual user. As a result, we allow practitioners to curate a catalog that best suits the needs of their patients. In our catalog's advanced search tool, you will find several of these third-party certifications that can be used for filtering when selecting products.

You can also learn more about each of the various certifications at **www.fullscript.com/hcp**.



These are some of the numerous third-party certifications you will find in the Fullscript catalog. Note that specific certifications can be applied for different reasons, so it's important to understand and determine what quality assurances are important to you.

Certification Mark	Organization	Description
	United States Pharmacopeia (USP)	The USP Dietary Supplement Verification Program is a voluntary third-party certification aimed at verifying the quality of finished products, ensuring what's on the label is in the bottle.
	International Organization for Standardization (ISO)	The International Organization for Standardization (ISO) is an independent, non-governmental organization responsible for developing standards for products, services and systems, to ensure quality, safety and efficiency.
NSF	National Sanitation Foundation (NSF)	The National Sanitation Foundation (NSF) works to develop public health standards and certification programs that help protect the world's food, water, consumer products and environment.
NSF. Lettite for sport	National Sanitation Foundation (NSF) Certified for Sport®	The NSF Certified for Sport is a third party certification program designed specifically for sport supplements to ensure products do not contain unsafe levels of contaminants, prohibited substances and masking agents.
USDA ORGANIC	USDA Organic	The National Organic Program (NOP), a program housed within the United States Department of Agriculture (USDA), is responsible for developing national standards for production, labeling and enforcement of all USDA organic products.
FAIRTRADE	Fair Trade	Fair Trade Certified, a third-party certification based on social, environmental and economic standard ensures that products are grown, harvested, manufactured and traded in ways that improve lives and protect the environment.
IFOS	The International Fish Oil Standards (IFOS)	IFOS is a third party certification program focusing exclusively on testing the purity, potency and freshness of omega-3 fish oil products.
VERIFIED	The Non-GMO Project	The Non-GMO Project is a non-profit organization offering a third-party non-GMO verification program that aims to support sources and practices that effectively minimize GMO risk to the supply chain.
Giuten-Free	Gluten-Free Certification Organization (GFCO)	GFCO is an industry program of the Gluten Intolerance Group (GIG), a non-profit organization that offers third- party certification to manufacturers of gluten-free products, including dietary supplements.
A WIED AND A	Vegan Action	Vegan Action, a non-profit organization, offers third-party certification to verify vegan claims, ensures that animals and animal by-products have not been used in the formulation or manufacturing of products and ensures that products have not been tested on animals.



Developing protocols

Protocol development in integrative medicine is typically not a simple process. Patients require individualized care, and what works for one patient may not work for another.

The Fullscript Integrative Medical Advisory team advises using an *evidence-informed* approach to protocol development. To simplify this process for practitioners, we have assembled a sampling of *evidence-based* standardized protocols that practitioners can use as a foundation when developing individualized protocols.

To establish these protocols, we first developed a rating scale to discern the rigor of evidence supporting a specific nutrient's therapeutic effect.

These protocols were developed using only A through D-quality evidence. The full rating scale is available at **www.fullscript.com/hcp**.

Class	Туре	Studies
Α	Systematic review or meta-analysis of human trials	N/A
В	Human RDBPC	≥ 2 studies and/ or 1 study with ≥ 50 subjects
С	Human RDBPC or RCT	1 study < 50 subjects

D Human trials or In-vivo animal trials

Please refer to the complete **Rating Scale** for further information.

i

For more protocols and a complete listing of the literature reviewed, visit our Integrative Clinical Education Hub at

www.fullscript.com/hcp

Disclaimer

The ingredients included in these protocols are based on a review of existing clinical research, with a priority placed on systematic reviews and meta-analyses, classified as A in the Rating Scale.

These protocols are intended to form a foundation for developing individualized treatment plans. Clinician discretion is highly advised, as ingredients can vary in safety and effectiveness, depending on the needs of the individual patient.





Irritable bowel syndrome

Peppermint (Mentha x piperita) oil

0.1-0.3 mL (or 200 mg), 3 times per day

- Significant reduction of abdominal pain and global symptoms, relative to placebo.
- Benefits no longer present two weeks after supplement cessation.

Soluble dietary fiber

20-35 g per day of long-chain, intermediate viscous, soluble and moderately fermentable dietary fiber

 Safe and effective in improving global IBS symptoms, relative to placebo.
 Note that short-chain, highly fermentable soluble fiber should be avoided as it can aggravate IBS symptoms.

Probiotics

25-50 billion CFU, 1-3 times per day

- Effective in reducing symptom and severity score in patients with IBS
- Current recommendations suggest using an equal dosage of lactobacillus and bifidobacterium species

Type 2 diabetes mellitus

Berberine

500 mg, 3 times per day, minimum 12 weeks

• In diabetic patients, demonstrated reduction in blood glucose levels comparable in effect to pharmaceutical interventions

Chromium picolinate

500 mcg, 2 times per day, minimum 4 weeks

- Current literature confirms a minor reduction in blood glucose when supplemented consistently for four weeks or longer
- Chromium supplements should be taken with a carbohydrate-containing meal

Psyllium husk

5 g, 3 times per day, minimum 6 weeks

- In diabetic patients, demonstrated minor to moderate reduction in blood glucose levels
- 15 g daily is a minimum dose and can be titrated up gradually to patient tolerance

For more protocols and a complete listing of the literature reviewed, visit our Integrative Clinical Education Hub at www.fullscript.com/hcp.

Osteoarthritis

Glucosamine

1.5 to 2 g per day, minimum 12 weeks

- Individual RDBPC studies consistently demonstrate reduction in pain and global symptoms of OA
- Combination with chondroitin may increase
 overall effectiveness

SAMe

1200 mg, 1-2 times per day, minimum 30 days

 Multiple RDBPC studies demonstrated comparable pain reduction to OTC pharmaceuticals like naproxen and nabumetone

Turmeric (Curcuma longa)

500 mg MERIVA, 2-4 times per day, minimum 30 days

- In small clinical trials (< 100 subjects), demonstrated effect in pain reduction, comparable to acetaminophen
- One recent review confirmed that both whole turmeric extract and curcumin demonstrated short-term reduction in pain

Additional promising interventions with preliminary evidence demonstrating reduction in OA symptoms include:

- Green-lipped mussel extract
- Indian Frankincense (Boswellia serrata)
- L-carnitine
- Natural Eggshell Membrane
- Pycnogenol
- Type II Collagen

Summary

The ingredients included in these protocols are based on a review of existing clinical research, with a priority placed on systematic reviews and meta-analyses, classified as A in the Rating Scale.

These protocols are intended to form a foundation for developing individualized treatment plans. Clinician discretion is still advised, as ingredients can vary in safety and effectiveness depending on the needs of the individual patient.

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