<2800> Multi-Ingredient Dietary Supplement Products – Development of Quality Tests

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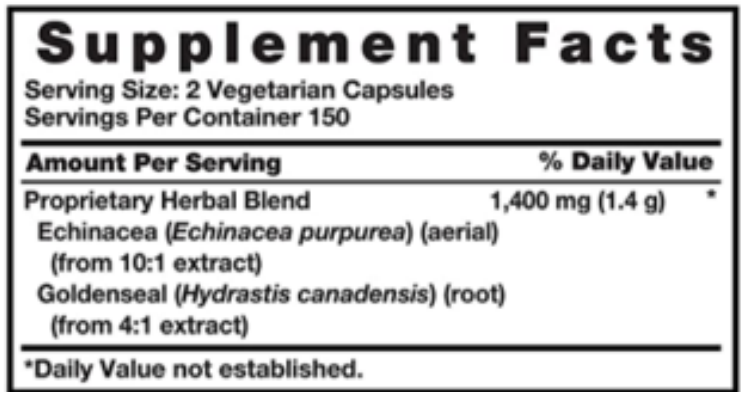
The standard of trust

Rationale for the general chapter

- Dietary supplements are subject to FDA cGMP requirements.
  - To comply with cGMP, dietary supplements manufacturers must establish product specifications for the identity, purity, strength, composition, and limits on types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary supplement.
  - The specifications that define the products, should consider the test methods with acceptance criteria against which conformity to specifications is assessed.
  - These test methods and acceptance criteria must be scientifically valid.
- The USP has received many questions about the applicability of existing monographs to multi-ingredient dietary supplement products.
- The USP hosted the Roundtable on Multi-Ingredient Dietary Supplement Products in October 2019 with representatives from the dietary supplements industry
  - It was recommended that a general chapter be developed to guide manufacturers on how to use USP resources for assessing the quality of multi-ingredient dietary supplement products

General chapter <2800>

- Examples of Multi-Ingredient Dietary Supplements

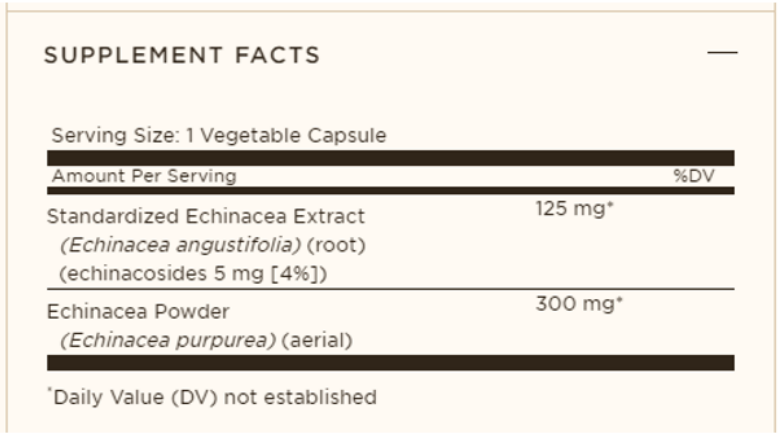


Supplement Facts

Serving Size: 2 Vegetarian Capsules
Servings Per Container 150

Amount Per Serving	% Daily Value
Proprietary Herbal Blend	1,400 mg (1.4 g) *
Echinacea (*Echinacea purpurea*) (aerial) (from 10:1 extract)	
Goldenseal (*Hydrastis canadensis*) (root) (from 4:1 extract)	

*Daily Value not established.

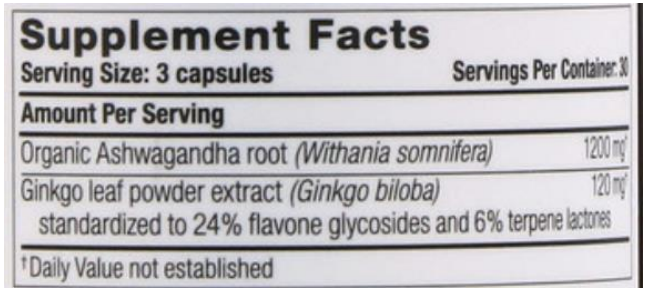


SUPPLEMENT FACTS

Serving Size: 1 Vegetable Capsule

Amount Per Serving	%DV
Standardized Echinacea Extract (*Echinacea angustifolia*) (root) (echinacosides 5 mg [4%])	125 mg*
Echinacea Powder (*Echinacea purpurea*) (aerial)	300 mg*

*Daily Value (DV) not established

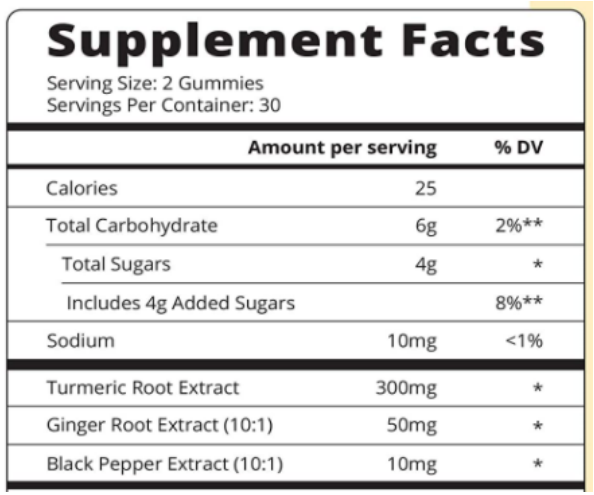


Supplement Facts

Serving Size: 3 capsules — Servings Per Container: 30

Amount Per Serving	
Organic Ashwagandha root (*Withania somnifera*)	1200 mg†
Ginkgo leaf powder extract (*Ginkgo biloba*) standardized to 24% flavone glycosides and 6% terpene lactones	120 mg†

†Daily Value not established



Supplement Facts

Serving Size: 2 Gummies
Servings Per Container: 30

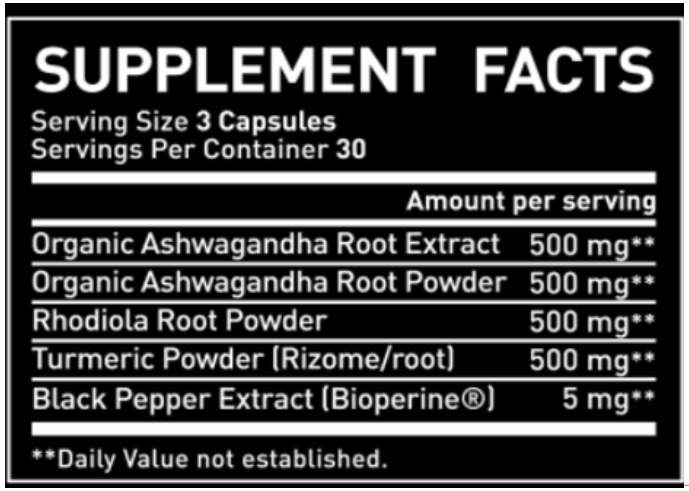
	Amount per serving	% DV
Calories	25	
Total Carbohydrate	6g	2%**
Total Sugars	4g	*
Includes 4g Added Sugars		8%**
Sodium	10mg	<1%
Turmeric Root Extract	300mg	*
Ginger Root Extract (10:1)	50mg	*
Black Pepper Extract (10:1)	10mg	*

Supplement Facts

Serving Size: 2 Vegetable Capsules
Servings Per Container: 30

Amount Per Serving	
Echinacea Extract (*Echinacea angustifolia*) [root]	50 mg*
Echinacea Extract (4:1) (*Echinacea purpurea*) [root]	150 mg*
Echinacea Powder (*Echinacea purpurea*) [aerial]	400 mg*
Cat's Claw Extract (3:1) (*Uncaria tomentosa*) [whole bark]	300 mg*

*Daily Value not established



SUPPLEMENT FACTS

Serving Size **3 Capsules**
Servings Per Container **30**

	Amount per serving
Organic Ashwagandha Root Extract	500 mg**
Organic Ashwagandha Root Powder	500 mg**
Rhodiola Root Powder	500 mg**
Turmeric Powder (Rizome/root)	500 mg**
Black Pepper Extract (Bioperine®)	5 mg**

**Daily Value not established.

General chapter <2800>

- Available compendial standards – starting point for development of quality tests for multi-ingredient dietary supplement products
  - Corresponding individual monographs
    - Definition (acceptance criteria)
    - Identification (Procedures + Acceptance criteria)
    - Composition/Strength (Quantitative analysis + Acceptance criteria)
    - Impurities (Procedures + Acceptance criteria)
    - Specific Tests (Procedures + Acceptance criteria)
    - Performance testing –for finished products (Procedures + Acceptance criteria)
  - General chapters (applicable in monographs + informational GC)
  - Corresponding Chemical Reference Standards (highly characterized materials demonstrated to have the appropriate qualities to support their intended use)
  - Corresponding supplementary information from Dietary Supplement Compendium (DSC) (Illustrations)

General chapter <2800>

- The content of the chapter has been structured with the understanding that DS products quality attributes fall into two categories.
  - Tests, analytical procedures, and acceptance criteria that assess general quality attributes
    - identification, strength, impurities, product weight variation, microbial content, and other specific tests depending on the nature of the product
  - Tests, analytical procedures, and acceptance criteria that evaluate in vitro product performance
    - disintegration or dissolution
      - to estimate the ability of the finished products to release dietary ingredients for potential absorption
      - to assess the lot-to-lot quality of a dietary supplement product
      - to ensure continuing product quality and performance after certain changes, such as changes in the composition, the manufacturing process, the site of manufacture, and the scale-up of the manufacturing process.
  - Appropriate recommendations are provided for methods development and validation

General chapter <2800>

- Provides guidelines on the development and application of the following quality tests for multi-ingredient dietary supplement products:
  - Universal Tests
    - Identification (TLC, HPTLC, HPLC, UPLC, GC, NMR)
      - If a single test lacks specificity two or more orthogonal tests should be used for identification
    - Strength (HPLC, UPLC, GC)
    - Impurities (organic impurities, inorganic impurities, residual solvents)
  - Specific Tests
    - Weight Variation (Capsules, tablets, Chewable Gels)
    - Deliverable Volume (Oral solutions)
    - Water Activity (Chewable gels)
    - pH (Chewable Gels, liquid (aqueous based) dietary supplement products)
    - Contaminants (microbial, environmental)
    - Other tests (may be required depending on the nature of the dietary ingredient and finished product)
    - Intentional Adulterants (sport, weight loss, sexual enhancement, etc.)
- Provides guidelines for application of the Performance Testing

Goals of the Open Forum

- Provide examples of principles for the development of quality tests for evaluating multi-ingredient dietary supplements using available compendial standards
  - Identification
    - “HPTLC for describing and controlling the quality of poly-herbal formulations”.
  - Strength
    - “USP monographs in a small contract laboratory: case studies”.
  - Performance Testing
    - “Applying Solubility and Permeability Properties of Botanical Markers for Performance Testing of Botanical Dietary Supplements: Challenges and Opportunities”
- Collect feedback from the Forum participants on what additional information might be useful to include in the chapter to improve the quality and relevance of the chapter before it is posted in Pharmacopeial Forum (PF) for public comments.

Thank You

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