#### **APPLICATIONS**

- Microbial Support
- Antioxidant Support
- Inflammatory Response Support



# **INTRODUCTION**

This product is a synergistic blend of Elecampane (*Inula helenium*) root, Jalapa (*Ipomoea purga*) root, Blackberry (*R. fruticosus*) leaves, and Capirona (*Calycophyllum spruceanum*) bark. It is designed to assist with comprehensive microbial support, with additional antioxidant support and healthy inflammatory response support.\*

Our liquid extracts are made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMP), as do our suppliers.

*I. helenium* belongs to the Asteraceae/Compositae family.¹ The root includes volatile oils such as alantolactone, isoalantolactone, alantol, alpha- and betabergamotene, beta-pinene, and anethole; amino acids such as aspartic acid, serine, threonine, and glutamic acid; sterols such as stigmasterol and beta-sitosterol; and thymol derivatives.²-⁴ Alantolactone and isoalantolactone are considered the main constituents.³,⁵ The main phenolic compounds that may help with antioxidant support are the phenolic acids (caffeic, dicaffeoyl quinic, chlorogenic, and hydroxybenzoic), terpenes (alantolactone and isoalantolactone), and flavonoids (epicatechin, catechin gallate, dihydroquercetin pentosyl rutinoside, quercetin-3-0-beta-glucopyranoside, ferulic acid-4-0-glucoside, and kaempherol-7-Odipentoside).⁶ The roots also include dietary fiber from fructooligosaccharides and inulin.ⁿ *I. helenium* root has been used in traditional Chinese health practices for gastrointestinal support, where it is known as tu mu xiang.\*³ *I. helenium* may help with microbial support, as determined by the agarwell diffusion method.\*³,9 It may also help with mycelial support.\*°

*Ipomoea purga* is commonly known as jalap root and belongs to the Convolvulaceae family. Synonyms for *I. purga* include *Ipomoea jalapa, Ipomoea schiedeana, Convolvulus officinalis, Convolvulus purga* and *Exogonium purga*.<sup>10-12</sup> *I. purga* is a climbing vine that is native to southern Mexico.12 The root has been used in traditional health practices to support gastrointestinal regularity, <sup>13</sup> with other potential benefits under current investigation.\* <sup>14</sup> Constituents of *I. purga* root include convolvulin, jalapine, caffeic acid, scopoletin, valeric acid, starch,

and tiglic acid. ^14,15 *I. purga* has a long history of traditional use for supporting healthy gastrointestinal regularity and maintaining healthy peristalsis.  $^{*10,13,14}$ 

*R. fruticosus* belongs to the Rosaceae family and is commonly known as blackberry. Synonyms for *R. fruticosus* include *R. plicatus*, *R. affinis*, *R. canadensis*, *R. millspaughii*, and *R. laciniatus*. <sup>16</sup> *R. fruticosus* leaves have been traditionally used for microbial support. <sup>\*17</sup> The leaves contain phenolic acids such as neo-chlorogenic acid, caffeic acid, gallic acid, p-coumaric acid, and ellagic acid; flavonols such as quercetin, quercetin-3-O-galactoside, quercetin-3-O-glucuronide, and kaempferol; flavan-3-ols such as catechin, epicatechin, and epicatechin gallate methyl gallate; ellagitannins such as sanguiin H-6/lambertianin C, and casuarinin; anthocyanins such as cyanidin-3-O-glucoside; and triterpene acids such as rubinic acid and rubusic acid. <sup>18,19</sup> They also contain tannins, villosin, gallic acid, and iron. <sup>17</sup> *R. fruticosus* may also help with microbial support, <sup>20</sup> antioxidant support, <sup>19,21</sup> healthy inflammatory response support, <sup>19</sup> neurological support, <sup>22</sup> and gastrointestinal support. <sup>\*23</sup>

*C. spruceanum* belongs to the Rubiaceae family and is commonly known as Capirona. A synonym for this plant is *Eukylista spruceana*. It is native to the Amazon rainforest and is sometimes called the Tree of Youth. It has been used in traditional health practices for healthy inflammatory response support. Constituents of *C. spruceanum* include seco-iridoids 6'-O-acetyldiderroside, 7-methoxydiderroside, 8-O-tigloyldiderroside, kingiside, secoxyloganin, and diderroside, as well as iridoids loganin and loganetin. Other constituents include gardenoside, cyanidin, 5-hydroxymorin, 5-hydroxy-6-methoxycoumarin-glucoside, and taxifolin. *C. spruceanum* may also help with antioxidant support.

## MICROBIAL SUPPORT

*I. helenium* may help with microbial support, as determined by the agar-well diffusion method.\*8,9 It may also help with mycelial support.\*9 *R. fruticosus* may also help with microbial support. The most robust microbial support occurs with the hydro-alcoholic leaf extract, as quantified by a 6-11 mm zone of inhibition.\*20

#### ANTIOXIDANT SUPPORT

*I. helenium* root extract may help with antioxidant support, as determined by DPPH, phosphomolybdenum, beta-carotene bleaching, ABTS, FRAP, and CUPRAC assays.\*7,8 Flavonoids are found in all plant parts, and the relevant phenolic compounds, concentrated in the inflorescence, leaves, and root, are highly soluble in ethanol.\*29 The constituent alantolactone may help to support levels of quinone reductase, glutathione S-transferase (GST), and glutathione reductase already within the normal range, in a dose-dependent manner.\*30 The antioxidant support of I. helenium is attributed to effects on PI3K and JNK signaling pathways, with support of Nrf2 already within the normal range.\*30

The phenolic content of *R. fruticosus has* been determined spectrophotometrically, and the free radical scavenging capacity was determined via DPPH assay.\*21 The constituent cyanidin-3-O-glucoside may provide particularly robust antioxidant support.\*19 *C. spruceanum* may also help with antioxidant support, as quantified by DPPH, ABTS, singlet oxygen, superoxide anion radical, and beta-carotene bleaching methods.\*26,27 In vivo antioxidant support was seen in *Caenorhabditis elegans* (C. elegans).\*26

#### INFLAMMATORY RESPONSE SUPPORT

Isoalantolactone, a sesquiterpene lactone found in I. helenium, may help with healthy inflammatory support.\*31 In vitro research has shown that isoalantolactone may help to maintain NF-kappa B already within the normal range.\*31 Alantolactone and isoalantolactone may help to maintain levels of IgE, TNF-alpha, and IFN-gamma already within the normal range.\*32 They may also help to maintain IL-4, IL-5 and IL-13 already within the normal range.\*32 Additionally, the sesquiterpene lactone igalan may help with healthy inflammatory support.\*33 R. fruticosus leaves contain cyanidin-3-Oglucoside which may help with healthy inflammatory response support by way of TNF-alpha and COX-2 inhibition.\*1

### SAFETY AND CAUTIONS

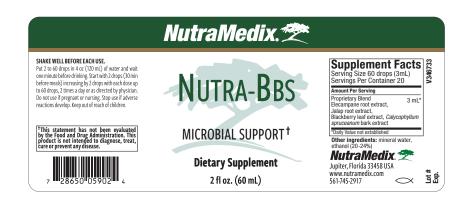
Information on the adverse effects of Inula helenium is limited. *I. helenium* may cause allergic reactions in those with allergies to other plants in the Asteraceae/ Compositae family, such as ragweed.<sup>34</sup> Cases of contact dermatitis have been reported, which may be attributed to the sesquiterpene lactones alantolactone and isoalantolactone. 35,36 I. helenium may have additive effects with CNS depressants.<sup>34</sup> Large amounts of I. helenium may cause vomiting and diarrhea.<sup>37</sup> Rarely, large amounts of I. helenium root may cause spasms or symptoms of paralysis.3

I. purga may cause purgative effects, which are contra-indicated in pregnancy. 38,39 It is also contraindicated in gastrointestinal inflammation or infection. 40 *I. purga* contains cathartic gluco-resins which may intensify peristalsis, increasing water elimination.<sup>13,41</sup> Consequently, it is contraindicated in those taking stimulant laxatives as it may have additive effects, leading to dehydration and electrolyte imbalance.<sup>42</sup> In addition, I. purga may have additive effects with diuretic-induced potassium loss. 42 Fluid and electrolyte imbalance may theoretically increase INR and risk of bleeding in those taking warfarin.<sup>10</sup> Electrolyte imbalance may also worsen the toxicity of cardiac glycosides.<sup>43</sup>

R. fruticosus is generally well tolerated. There is little information available on potential side effects. Insufficient data is available to determine the safety of *R. fruticosus* leaf in pregnancy.16 Data is currently limited for *C.* spruceanum, which has shown no evidence of toxicity in mice. 44

Safety not documented in breastfeeding or pregnant women, or in children under 3 years of age due to insufficient safety research.

\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.



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