

Receptor Detox

Support for Hormone Receptor Functionality to Help Foster Healthy Hormone Signaling

Receptor Detox contains carefully selected nutrients shown to gently, effectively and safely optimize hormone receptor function, ensuring healthy hormone signaling. Receptor dysfunction can be multifactorial; often a result of such things as systemic inflammatory responses, reactive oxygen species, endocrine disrupting compounds (EDCs), polymorphisms in receptor genes, signaling pathway anomalies, and altered gene expression.^{1,2,3} Long-term exposure to any or all of these contributing factors is widely thought to play an important role in many chronic conditions by modulating both hormone actions and hormone receptor activity.^{4,5,6} This product is recommended daily for optimal receptor functioning for both females and males, and highly recommended for mature people on hormone replacement.

Receptor Detox formulator, Dr. Devaki Lindsey Berkson, has worked as a hormone scholar at a Tulane University estrogen think-tank (Center for Bioenvironmental Research) with scientists who discovered the first two estrogen receptors, estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ). Dr. Berkson developed **Receptor Detox** to provide the most critical nutrients designed to help improve receptor functionality, restoring the tightly controlled regulation of endocrine activity disrupted by the modern environment. Her focus on receptor function and *not just hormone levels* is partly a result of many lectures delivered over years of E.Hormone conferences, which highlighted the role of receptor functionality in keeping hormone signals intact, and the role of receptor function in disease prevention.

Clinical Relevance

As the number of EDCs in production increase each year, so too does the number of conditions for which these environmental toxins are implicated, driving the pathophysiology, in part by blocking and/or mimicking hormones as well as disturbing hormone receptor function.



One mechanism is by competitive inhibition of hormone receptors, which displaces endogenous hormones and results in altered nuclear signaling.

Perfluorooctanoic acid (PFOA), for example, has been shown to compete with calcitriol for the vitamin D receptor, altering the receptor's structure and flexibility, and altering the response of vitamin D-responsive genes as well as osteoblastic function. Not only may this provide a mechanism for the inverse relationship between perfluorinated compounds and bone health, but serum levels of vitamin D among exposed men were not affected, while parathyroid levels were increased. This provides a solid demonstration of the ability of environmental toxins to impair receptor function, contribute to disease, while not altering the level of hormones (such as vitamin D) which would normally be used to assess risk.⁷

Having a daily receptor detox on board may be increasingly important, given the ubiquity of EDCs and their associated conditions. While insulin resistance is the most well-characterized example of receptor resistance, nearly every hormone (thyroxine, testosterone, progesterone, etc.) can be affected.^{8,9,10} Adipose tissue is also an active endocrine organ, modulating appetite control, inflammation, insulin sensitivity, etc., and is also targeted by EDCs, likely contributing to both the obesity and diabetes epidemics.¹¹



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com • www.bioticsresearch.com

Receptor Detox supplies key nutrients which:

1. Allow hormones to bind effectively and appropriately to their associated receptors.
2. Clear competitive inhibitors off receptors in a safe and continuous manner.
3. Optimize receptor functionality, allowing hormones to safely and effectively deliver their signals and overcome resistance

Highlights

Vitamin B3 (niacin & niacinamide)

Vitamin B3 is required for the synthesis of nicotinamide adenine dinucleotide (NAD), an essential co-factor for the enzymes which produce all active steroid hormones, known as 3 β -hydroxysteroid dehydrogenase isozymes.¹² These enzymes synthesize glucocorticoids, mineralocorticoids, progesterone, androgens, and estrogens, and are found in a variety of tissues, including the adrenal glands, ovaries, and testes.¹³

Niacin also binds to the G-protein-coupled receptor HCAR2 (Hydroxycarboxylic acid receptor 2), expressed in microglia, adipocytes, macrophages, keratinocytes, etc., reducing inflammation in the gastrointestinal and nervous systems, enhancing synthesis of IgA in the intestine, and promoting cutaneous vasodilation (flushing).^{14,15,16} The broad multi-system anti-inflammatory effects of niacin, mediated via modulation of G-protein coupled receptors, may help to explain the cardiovascular benefits previously attributed solely to a reduction in lipids.¹⁷

Vitamin B6

Vitamin B₆ is recognized to modify both the expression and the action of steroid hormone receptors, and to be essential for catecholamine synthesis, including neurotransmitters such as serotonin. Very recently it has been shown to upregulate glutathione production and Nrf2 transactivation, a pathway associated with cellular protection and defense.¹⁸

Also, the more rapid utilization of B₆ in the presence of excess estrogen or estrogen-like compounds increases nutritional needs.¹⁹ A lack of the active form of B6 and other methyl donors may predispose for excessive estrogen activity, heightening the risk for estrogen-associated dysfunction.²⁰ **Receptor Detox** provides the active form of vitamin B₆, pyridoxal-5-phosphate, avoiding any biochemical bottlenecks which may limit its benefit.

Calcium-d-glucarate

Calcium-d-glucarate provides support for glucuronidation, a key type of phase 2 detoxification needed for many exogenous toxins as well as endogenous compounds, including bilirubin and steroid hormones.²¹

After modification by the intestinal microbiome, calcium-d-glucarate's metabolites inhibit the enzyme beta-glucuronidase, thereby preventing the deconjugation of glucuronic acid from these substrates, and improving their elimination. Enhancing glucuronidation modulates the cellular hormonal milieu by supporting the healthy detoxification of excess estrogen and other steroids.^{22,23}

In addition to enhancing the removal of excess hormones, calcium-d-glucarate also provides support for the detoxification of many hormone-mimicking environmental toxins. For example, PCBs and phthalates, both established as endocrine disruptors, undergo phase 2 biotransformation via glucuronidation before being eliminated.^{24,25} Indeed, genetic variants in glucuronidation enzymes in combination with exposure to endocrine disrupting chemicals have been associated with risk for hormone-sensitive conditions, such as polycystic ovary syndrome.²⁶

Iodine

Iodine promotes detoxification, lymph flow and offers protection to the receptor. It helps lower to responsiveness of breast tissue to sex steroids due to its antioxidant and antiproliferative effects, contributing to the integrity of normal mammary glands.^{27,28,29} Iodine exhibits antiproliferative and apoptotic effects in various cancer cells including the breast. In animal and human studies, molecular iodine (I₂) supplementation limits excessive cell growth.³⁰ Specifically, I₂ supplementation enhances the formation of 6-iodolactone (6-IL), a potent promoter of peroxisome proliferator-activated receptor gamma (PPAR γ) expression, partly responsible for an induction of apoptosis and inhibition of several estrogen-responsive genes.³¹ Iodine also plays a role in estrogen metabolism.

In addition, sufficient iodine avoids and protects the build-up of endocrine-disrupting "halides," which are competitive inhibitors of iodine found in bakery products, flame retardants, pesticides, insecticides and our water supply.³²

Cilantro

Cilantro helps to remove EDCs out of endocrine tissues. A natural chelating agent against heavy metals, cilantro helps move toxic substances through the kidneys and out of the body.^{33,34,35,36} *In vitro* studies also suggest it has antioxidant and antiproliferative effects.^{37,38}

Parsley

Parsley contains unique flavonoids with antioxidant and anti-inflammatory properties. Apigenin, the bioactive flavone found in parsley, has been shown to act as a powerful antioxidant and enhance TRAIL-mediated apoptosis in irregular cells.³⁹ It also appears to have direct effects on the estrogen receptor, with *in vitro* data demonstrating an inhibition of cervical growth by inhibiting an estrogen receptor mediated pathway.⁴⁰

Together with chlorella and dandelion, parsley works to promote healthy detoxification and elimination of endogenous and exogenous compounds.

Zinc

Zinc is an essential nutrient in all sex steroid binding domains. It is required by zinc finger protein domains, and a deficiency has been shown to increase the oxidative stress and alter the architecture of mammary tissues, creating a toxic microenvironment in animal studies.^{41,42,43,44}

Magnesium

Magnesium glycinate, along with zinc citrate, pyridoxal-5-phosphate, selenium and milk thistle, all promote hepatic detoxification of hormones and elimination of toxins that block receptor functionality.

Magnesium also helps regulate sex hormone binding globulin (SHBG), improving testosterone signaling.^{45,46}

Milk Thistle

Primarily recognized for its hepatoprotective and antioxidant properties, milk thistle contains flavonoids, which limit excessive cellular reproduction through multiple mechanisms in both *in vitro* and *in vivo* models, including modulation of the ER α receptor and suppression of TGF- β 2 production.^{47,48,49,50} Recently, milk thistle has also been found to selectively bind the ER β receptor, providing additional protection to estrogen sensitive tissues.^{51,52}

Summary & Recommendations

Receptor Detox supports healthy hormonal and neurotransmitter signaling, and mineral displacement of EDCs and heavy metals, allowing for optimal receptor functionality. Key minerals and botanicals improve receptor function and enhance the detoxification and elimination of the environmental pollutants which have become commonplace, competing with endogenous hormone activity.

Dietary Support

In addition to **Receptor Detox** supplementation, consuming Brassica vegetables daily helps to:

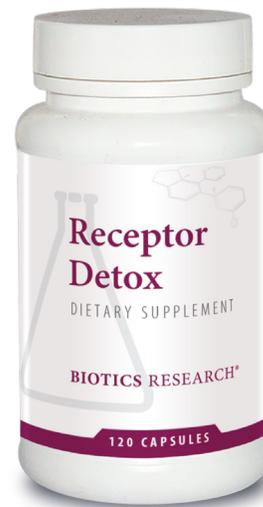
- Detoxify carcinogens
- Keep estrogens safe
- Promote balance between ER α and ER β
- Inhibit growth and activity of tumors
- Activate antioxidants
- Support healthy inflammation, including the resolution of inflammation

Recommended Use: Two capsules two times per day with food as a dietary supplement or as otherwise directed by a healthcare professional.

Additional dosing suggestions

For a deeper detox, take four capsules twice a day. Also, before initiating hormonal therapies, it is recommended to take four capsules twice a day for a week and then continue with two capsules twice a day while taking hormones.

Caution: Not recommended for children, pregnant or lactating women.



Receptor Detox is available in a 120 capsule bottle (#6271).

Supplement Facts

Serving Size: 2 Capsules
Servings Per Container: 60

	Amount Per Serving	% Daily Value
Niacin (as niacin and niacinamide)	40 mg	250%
Vitamin B6 (as pyridoxal-5-phosphate)	10 mg	588%
Iodine (as potassium iodide)	2 mg	1,333%
Magnesium (as magnesium glycinate)	5 mg	<2%
Zinc (as zinc citrate)	10 mg	91%
Selenium (as vegetable culture†)	50 mcg	91%
Calcium d-glucarate	100 mg	*
Proprietary Blend	710 mg	
Cilantro (Coriandrum sativum)(seed)(extract)*, Dandelion (Taraxacum officinale)(root)(extract)*, Parsley (Petroselinum crispum)(leaf)(extract)*, Chlorella (cracked cell wall)*, Milk thistle (Silybum marianum)(root & aerial part)(extract)*		

*Daily Value not established

Other ingredients: Capsule shell (gelatin and water) and stearic acid (vegetable source).
† Specially grown, biologically active vegetable culture (from organic peas, lentils and/or chickpeas) containing **Phytochemically Bound Selenium™** and other phytochemicals including polyphenolic compounds with SOD and catalase, dehydrated at low temperature to preserve associated enzyme factors.

This product is gluten and dairy free.

RECOMMENDATION: Two (2) capsules, two (2) times per day with food as a dietary supplement or as otherwise directed by a healthcare professional.

CAUTION: Not recommended for children, pregnant or lactating women.

References

- Amir S, Shah STA, Mamoulakis C, et al. Endocrine Disruptors Acting on Estrogen and Androgen Pathways Cause Reproductive Disorders through Multiple Mechanisms: A Review. *Int J Environ Res Public Health*. 2021 Feb 4;18(4):1464. PMID: 33557243
- Marquardt RM, Kim TH, Shin JH, Jeong JW. Progesterone and Estrogen Signaling in the Endometrium: What Goes Wrong in Endometriosis? *Int J Mol Sci*. 2019 Aug 5;20(15):3822. PMID: 31387263
- Farrugia F, Aquilina A, Vassallo J, et al. Bisphenol A and Type 2 Diabetes Mellitus: A Review of Epidemiologic, Functional, and Early Life Factors. *Int J Environ Res Public Health*. 2021 Jan 15;18(2):716. PMID: 33467592
- Attina TM, Malits J, Naidu M, et al. Racial/ethnic disparities in disease burden and costs related to exposure to endocrine-disrupting chemicals in the United States: an exploratory analysis. *J Clin Epidemiol*. 2019 Apr;108:34-43. PMID: 30529005
- Calaf GM, Ponce-Cusi R, Aguayo F, et al. Endocrine disruptors from the environment affecting breast cancer. *Oncol Lett*. 2020 Jul;20(1):19-32. PMID: 32565930
- Cardenas A, Hivert MF, Gold DR, et al. Associations of Perfluoroalkyl and Polyfluoroalkyl Substances With Incident Diabetes and Microvascular Disease. *Diabetes Care*. 2019 Sep;42(9):1824-1832. PMID: 31296647
- Di Nisio A, Rocca MS, De Toni L, et al. Endocrine disruption of vitamin D activity by perfluoro-octanoic acid (PFOA). *Sci Rep*. 2020 Oct 8;10(1):16789. PMID: 33033332
- Patel BG, Rudnicki M, Yu J, et al. Progesterone resistance in endometriosis: origins, consequences and interventions. *Acta Obstet Gynecol Scand*. 2017 Jun;96(6):623-632. PMID: 28423456
- Calaf GM, Ponce-Cusi R, Aguayo F, et al. Endocrine disruptors from the environment affecting breast cancer. *Oncol Lett*. 2020 Jul;20(1):19-32. PMID: 32565930
- Coperchini F, Awwad O, Rotondi M, et al. Thyroid disruption by perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA). *J Endocrinol Invest*. 2017 Feb;40(2):105-121. PMID: 27837466
- Dirinck EL, Dirlu AC, Govindan M, et al. Exposure to persistent organic pollutants: relationship with abnormal glucose metabolism and visceral adiposity. *Diabetes Care*. 2014 Jul;37(7):1951-8. PMID: 24963112
- Makarov MV, Trammell SAJ, Migaud ME. The chemistry of the vitamin B3 metabolome. *Biochem Soc Trans*. 2019 Feb 28;47(1):131-147.
- Goswami AM. Structural modeling and in silico analysis of non-synonymous single nucleotide polymorphisms of human 3 β -hydroxysteroid dehydrogenase type 2. *Meta Gene*. 2015 Aug 8;5:162-72.
- Giri B, Belanger K, Seamon M, et al. Niacin Ameliorates Neuro-Inflammation in Parkinson's Disease via GPR109A. *Int J Mol Sci*. 2019 Sep 14;20(18):4559.
- Gong Y, Jin X, Yuan B, et al. G Protein-Coupled Receptor 109A Maintains the Intestinal Integrity and Protects Against ETEC Mucosal Infection by Promoting IgA Secretion. *Front Immunol*. 2021 Jan 8;11:583652.
- Tuteja S. Activation of HCAR2 by niacin: benefits beyond lipid lowering. *Pharmacogenomics*. 2019 Nov;20(16):1143-1150.
- Graff EC, Fang H, Wanders D, et al. Anti-inflammatory effects of the hydroxycarboxylic acid receptor 2. *Metabolism*. 2016 Feb;65(2):102-13.
- Wei Y, Lu M, Mei M, et al. Pyridoxine induces glutathione synthesis via PKM2-mediated Nrf2 transactivation and confers neuroprotection. *Nat Commun*. 2020 Feb 18;11(1):941. PMID: 32071304
- Wilson MP, Plecko B, Mills PB, et al. Disorders affecting vitamin B6 metabolism. *J Inher Metab Dis*. 2019 Jul;42(4):629-646. PMID: 30671974.
- Agnoli C, Groni S, Krogh V, et al. Plasma Riboflavin and Vitamin B-6, but Not Homocysteine, Folate, or Vitamin B-12, Are Inversely Associated with Breast Cancer Risk in the European Prospective Investigation into Cancer and Nutrition-Varese Cohort. *J Nutr*. 2016 Jun;146(6):1227-34. PMID: 27121532
- Dwivedi C, Heck WJ, Downie AA, et al. Effect of calcium gluconate on beta-glucuronidase activity and gluconate content of certain vegetables and fruits. *Biochem Med Metab Biol*. 1990 Apr;43(2):83-92.
- Hanausek M, Walaszek Z, Slaga TJ. Detoxifying cancer causing agents to prevent cancer. *Integr Cancer Ther*. 2003 Jun;2(2):139-44.
- Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *J Nutr Metab*. 2015;2015:760689.
- Silva MJ, Barr DB, Reidy JA, et al. Glucuronidation patterns of common urinary and serum monobest phthalate metabolites. *Arch Toxicol*. 2003 Oct;77(10):561-7.
- Dhakal K, Gadupudi GS, Lehmler HJ, et al. Sources and toxicities of phenolic polychlorinated biphenyls (OH-PCBs). *Environ Sci Pollut Res Int*. 2018 Jun;25(17):16277-16290.
- Luo Y, Nie Y, Tang L, et al. The correlation between UDP-glucuronosyltransferase polymorphisms and environmental endocrine disruptors levels in polycystic ovary syndrome patients. *Medicine (Baltimore)*. 2020 Mar;99(11):e19444.
- Eskin BA, Bartuska DG, Dunn MR, Jacob G, Dratman MB. Mammary gland dysplasia in iodine deficiency. Studies in rats. *JAMA*. 1967 May 22;200(8):691-5. PMID: 6071498
- Eskin BA, Sparks CE, Lamont BI. The intracellular metabolism of iodine in carcinogenesis. *Biol Trace Elem Res*. 1979 Jun;1(2):101-17. PMID: 24277065.
- Aceves C, Anguiano B, Delgado G. Is iodine a gatekeeper of the integrity of the mammary gland? *J Mammary Gland Biol Neoplasia*. 2005 Apr;10(2):189-96. PMID: 16025225.
- Cuenca-Micó O, Aceves C. Micronutrients and Breast Cancer Progression: A Systematic Review. *Nutrients*. 2020 Nov 25;12(12):3613. PMID: 33255538
- Aceves C, García-Solis P, Arroyo-Helguera O, et al. Antineoplastic effect of iodine in mammary cancer: participation of 6-iodolactone (6-IL) and peroxisome proliferator-activated receptors (PPAR). *Mol Cancer*. 2009 Jun 6:8:33. PMID: 19500378
- Halka M, Smoleń S, Czernicka M, et al. Iodine biofortification through expression of HMT, SAMT and S3H genes in *Solanum lycopersicum* L. *Plant Physiol Biochem*. 2019 Nov;144:35-48. PMID: 31557638
- Evaluation of the Chelating Effect of the Methanolic Extract of *Coriandrum sativum* and its Fractions on Wistar Rats Poisoned with Lead Acetate. *Afr J Tradit Complement Altern Med*. 2017 Jan 13;14(2):92-102.
- Acar T, Kaya E, Yoruk MD, et al. Changes in tissue gadolinium biodistribution measured in an animal model exposed to four chelating agents. *Jpn J Radiol*. 2019 Jun;37(6):458-465. PMID: 30929137.
- Rodrigues KE, de Oliveira FR, Barbosa BR, et al. Aqueous *Coriandrum sativum* L. extract promotes neuroprotection against motor changes and oxidative damage in rat progeny after maternal exposure to methylmercury. *Food Chem Toxicol*. 2019 Nov;133:110755. PMID: 31408720.
- Khan AZ, Ding X, Khan S, et al. Biochar efficacy for reducing heavy metals uptake by Cilantro (*Coriandrum sativum*) and spinach (*Spinacia oleracea*) to minimize human health risk. *Chemosphere*. 2020 Apr;244:125543. PMID: 32050340.
- Tang EL, Rajarajeswaran J, Fung SY, Kanthimathi MS. Antioxidant activity of *Coriandrum sativum* and protection against DNA damage and cancer cell migration. *BMC Complement Altern Med*. 2013 Dec 9;13:347. PMID: 24517259
- Prachayasittikul V, Prachayasittikul S, et al. Coriander (*Coriandrum sativum*): A promising functional food toward the well-being. *Food Res Int*. 2018 Mar;105:305-323. PMID: 29433220
- Chang-Hee Kang, Ilandarage Menu Neelaka Molagoda, yung Hyun Choi, et al. Apigenin promotes TRAIL-mediated apoptosis regardless of ROS generation. *Food Chem Toxicol*. 2018 Jan;111:623-630. PMID: 29247770
- Zhang E, Zhang Y, Fan Z, Cheng L, Han S, Che H. Apigenin Inhibits Histamine-Induced Cervical Cancer Tumor Growth by Regulating Estrogen Receptor Expression. *Molecules*. 2020 Apr 23;25(8):1960. PMID: 32340124
- Bostanci Z, Mack RP Jr, Lee S, et al. Paradoxical zinc toxicity and oxidative stress in the mammary gland during marginal dietary zinc deficiency. *Reprod Toxicol*. 2015 Jul;54:84-92. PMID: 25088245
- Green S, Chambon P. Oestradiol induction of a glucocorticoid-responsive gene by a chimaeric receptor. *Nature*. 1987 Jan 1-7;325(6099):75-8. PMID: 3025750.
- Laity JH, Lee BM, Wright PE. Zinc finger proteins: new insights into structural and functional diversity. *Curr Opin Struct Biol*. 2001 Feb;11(1):39-46. PMID: 11179890.
- Wang W, Cai J, Lin Y, et al. Zinc fingers function cooperatively with KRAB domain for nuclear localization of KRAB-containing zinc finger proteins. *PLoS One*. 2014 Mar 19;9(3):e92155. PMID: 24647005
- Schreier B, Höcker B. Engineering the enolase magnesium II binding site: implications for its evolution. *Biochemistry*. 2010 Sep 7;49(35):7582-9. PMID: 20690637.
- Excoffon L, Guillaume YC, Woronoff-Lemsi MC, et al. Magnesium effect on testosterone-SHBG association studied by a novel molecular chromatography approach. *J Pharm Biomed Anal*. 2009 Feb 20;49(2):175-80. PMID: 19095394.
- Cheung CW, Gibbons N, Johnson DW, et al. Silibinin—a promising new treatment for cancer. *Anticancer Agents Med Chem*. 2010 Mar;10(3):186-95. PMID: 20015009.
- Binienda A, Ziolkowska S, Pluciennik E. The Anticancer Properties of Silibinin: Its Molecular Mechanism and Therapeutic Effect in Breast Cancer. *Anticancer Agents Med Chem*. 2020;20(15):1787-1796. PMID: 31858905.
- Principi M, Di Leo A, Pricci M, et al. Phytoestrogens/insoluble fibers and colonic estrogen receptor β : randomized, double-blind, placebo-controlled study. *World J Gastroenterol*. 2013 Jul 21;19(27):4325-33. PMID: 23885143
- Zheng N, Liu L, Liu WW, et al. Crosstalk of ROS/RNS and autophagy in silibinin-induced apoptosis of MCF-7 human breast cancer cells in vitro. *Acta Pharmacol Sin*. 2017 Feb;38(2):277-289. PMID: 27867187
- Liu W, Ji Y, Sun Y, Si L, et al. Estrogen receptors participate in silibinin-caused nuclear translocation of apoptosis-inducing factor in human breast cancer MCF-7 cells. *Arch Biochem Biophys*. 2020 Aug 15;689:108458. PMID: 32524997
- Dupuis ML, Conti F, Maselli A, et al. The Natural Agonist of Estrogen Receptor β Silibinin Plays an Immunosuppressive Role Representing a Potential Therapeutic Tool in Rheumatoid Arthritis. *Front Immunol*. 2018 Aug 17;9:1903. PMID: 30174672



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(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com • www.bioticsresearch.com