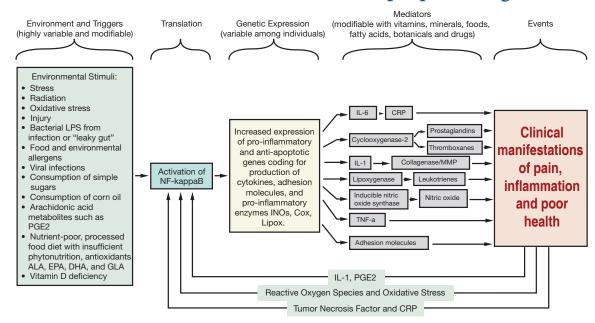
## Inflammation is a Destructive and Self-perpetuating Process



## An effective combination of these products may reduce the activation of NF-kappaB, thereby modifying inflammatory pathways.

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(800) 231-5777

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

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Synergistic Inhibition of NF-kappaB as an Underlying Scientific Basis for Phytonutritional Supplementation and Dietary Modification of Inflammatory Pathways

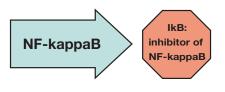


Alex Vasquez, DC, ND, DO

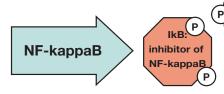
- 1. NF-kappaB is a molecule inside each cell that promotes pain and inflammation, and is associated with auto-immune and other unwanted health conditions.
- 2. Inhibition of NF-kappaB is emerging as a primary goal for the reduction of pain and inflammation.
- 3. Several natural products safely and effectively inhibit NF-kappaB, and they can be used in combination to help doctors attain improved outcomes in their patients.
- 4. Application of this research is simple:
  - a. low-fat, low-sugar diet
  - b. daily use of
    - i. **Bio-D-Mulsion Forte™**: 1-2 drops per day •
    - ii. **KappArest™**: 4 caps 2 times per day
    - iii. Optimal EFAs®: 1-3 caps per day

These products work together to promote optimal health.

New research is showing that many inflammatory health problems are associated with inappropriate activation of **nuclear transcription factor kappaB**, generally referred to as NF-kappaB. Therefore, inhibition of NF-kappaB is now a major goal towards improving the well-being of patients.<sup>1</sup>

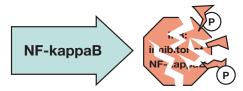


In the cytosol, NF-kappaB is made "inactive" by inhibitor kappaB.

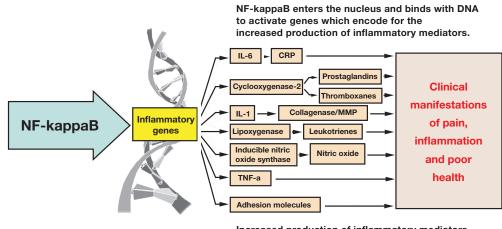


IKK: IkB kinase (alpha, beta, and gamma)

Exposure to "stressful stimuli" such as LPS or oxidative stress, activates "inhibitory kappaB kinase", which phosphorylates IkB for destruction.



Once IkB is destroyed, then NF-kappaB is free to bind with DNA.



Increased production of inflammatory mediators
- such as cytokines, prostaglandins, and leukotrienes promotes cellular dysfunction and tissue destruction.

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## Natural Interventions that Inhibit NF-kappaB

Bio-D-Mulsion Forte®	Quote/example from the research literature
vitamin D	<ul> <li>"1Alpha,25-dihydroxyvitamin D3 (1,25-(OH)2-D3), the active metabolite of vitamin D, can inhibit NF-kappaB activity in human MRC-5 fibroblasts, targeting DNA binding of NF-kappaB but not translocation of its subunits p50 and p65."<sup>2</sup></li> <li>"Thus, 1,25(OH)2D3 may negatively regulate IL-12 production by downregulation of NF-kappaB activation and binding to the p40-B sequence."<sup>3</sup></li> <li>Clinical studies have documented the benefits of vitamin D consumption, including studies of those with critical conditions.</li> </ul>

KappArest™	Quote/example from the research literature
Turmeric-curcumin (requires piperine for absorption)	• "Curcumin, EGCG and resveratrol have been shown to suppress activation of NF-kappaB."
Lipoic Acid	• "ALA reduced the TNF-alpha-stimulated ICAM-1 expression in a dose-dependent manner, to levels observed in unstimulated cells. Alpha-lipoic acid also reduced NF-kappaB activity in these cells in a dose-dependent manner." 5
Green tea extract	• "In conclusion, EGCG is an effective inhibitor of IKK activity. This may explain, at least in part, some of the reported anti-inflammatory effects of green tea."
Rosemary	• "These results suggest that carnosol suppresses the NO production and iNOS gene expression by inhibiting NF-kappaB activation, and provide possible mechanisms for its anti-inflammatory and chemopreventive action."
Grape seed extract	• "Constitutive and TNF-alpha-induced NF-kappaB DNA binding activity was inhibited by GSE at doses > or =50 microg/ml and treatments for > or =12 h."8
Propolis	"Caffeic acid phenethyl ester (CAPE) is an anti-inflammatory component of propolis (honeybee resin). CAPE is reportedly a specific inhibitor of nuclear factor-kappaB (NF-kappaB)."    CAPE   CAP
Resveratrol	<ul> <li>"Resveratrol's anti-inflammatory and growth-modulatory effects may thus be partially ascribed to the inhibition of activation of NF-kappaB and AP-1 and the associated kinases."         <ul> <li>"Both resveratrol and quercetin inhibited NF-kappaB-, AP-1- and CREB-dependent transcription to a greater extent than the glucocorticosteroid, dexamethasone."</li> </ul> </li> </ul>
Phytolens® (Biotics Research Corp. exclusive patent)	Phytolens® is Biotics Research Corporation's patented polyphenolic extract from lentils.     Published research has documented that Phytolens® exhibits broad-based antioxidant properties, is a free radical scavenger, and shows beneficial affects on inflammatory processes.  12

Optimal EFAs®	Findings from the research literature
ALA	• "CONCLUSIONS: Dietary supplementation with ALA for 3 months significantly decreases CRP, SAA and IL-6 levels in dyslipidaemic patients. This effect may provide a possible additional mechanism for the beneficial effect of plant n-3 polyunsaturated fatty acids in support of coronary and cardiac health." 13
EPA and DHA	<ul> <li>EPA-derived eicosanoid properties include the reduction in the production of proinflammatory eicosanoids such as LT-B4, PAFs, and cytokines such as TNF-alpha and IL-1, as well as a large reduction in PG-E2 and TX-B2.<sup>14</sup></li> <li>DHA, like EPA, is an important component of cell membranes. DHA functions by improving receptor function and signal transduction. Bioactive metabolites of DHA (docosatrienes and resolvins) mediate potent anti-inflammatory benefits<sup>15</sup>, and DHA appears essential for optimal cognitive function.<sup>16</sup></li> </ul>
GLA	GLA is the "health-promoting" n-6 fatty acid. GLA's benefits rely on its elongation to the biologically active DGLA from which eicosanoids that have cardioprotective and anti-inflammatory benefits are derived.  17,18

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