

Title	First Inventor/Author	Other Inventors/Authors	Publication Date	Language	Document Type	Journal Name	Abstract
Role of the GABA(B) receptor system in alcoholism and stress: focus on clinical studies and treatment perspectives.	Addolorato, Giovanni	Leggio, Lorenzo; Cardone, Silvia; Ferrulli, Anna; Gasbarrini, Giovanni	2009-11	English	Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't	Alcohol	Alcoholism and stress share some common neurobiological circuits, including the GABAergic system. In particular, the GABA(B) receptor seems to play an important role. The GABA(B) receptor agonist baclofen has been studied as a treatment for alcohol-dependent subjects. Baclofen administration in alcohol-dependent patients was able to promote abstinence, inducing the remission of withdrawal symptoms, reducing alcohol craving, and reducing alcohol intake. Baclofen also reduced anxiety in alcohol-dependent subjects, probably acting on brain stress circuitry and/or on other neuroendocrine systems. Baclofen also showed excellent safety and tolerability, even in alcohol-dependent patients with advanced liver disease (i.e., cirrhosis). Future studies should investigate which alcoholic subtype may better benefit of the administration of baclofen in the treatment of alcohol dependence.
Relaxation and immunity enhancement effects of gamma -Aminobutyric acid (GABA) administration in humans	Abdou, A. M.	Higashiguchi, S.; Horie, K.; Kim, M.; Hatta, H.; Yokogoshi, H.	2006	English	Journal Article	BioFactors	The effect of orally administrated gamma -Aminobutyric acid (GABA) on relaxation and immunity during stress has been investigated in humans. Two studies were conducted. The first evaluated the effect of GABA intake by 13 subjects on their brain waves. Electroencephalograms (EEG) were obtained after 3 tests on each volunteer as follows: intake only water, GABA, or L-theanine. After 60 minutes of administration, GABA significantly increases alpha waves and decreases beta waves compared to water or L-theanine. These findings denote that GABA not only induces relaxation but also reduces anxiety. The second study was conducted to see the role of relaxant and anxiolytic effects of GABA intake on immunity in stressed volunteers. Eight acrophobic subjects were divided into 2 groups (placebo and GABA). All subjects were crossing a suspended bridge as a stressful stimulus. Immunoglobulin A (IgA) levels in their saliva were monitored during bridge crossing. Placebo group showed marked decrease of their IgA levels, while GABA group showed significantly higher levels. In conclusion, GABA could work effectively as a natural relaxant and its effects could be seen within 1 hour of its administration to induce relaxation and diminish anxiety. Moreover, GABA administration could enhance immunity under stress conditions.
The effects of a nonbenzodiazepine GABA(A)R modulator on activity, metabolism, and anxiety in rats	Wideman, C. H.	Murphy, H. M.	2010	English	Meeting	Society for Neuroscience Abstract Viewer and Itinerary Planner	
Oral administration of gamma-aminobutyric acid and gamma-oryzanol prevents stress-induced hypoadiponectinemia	Ohara, Kazuyuki	Kiyotani, Yuka; Uchida, Asako; Nagasaka, Reiko; Maehara, Hiroyuki; Kanemoto, Shigeharu; Hori, Masatoshi; Ushio, Hideki	JUN 15 2011	English	Article	Phytomedicine (Jena)	Metabolic syndrome is a cluster of risk factors including insulin resistance and type 2 diabetes and is found to associate partly with chronic stress at work in human. Adiponectin circulates in mammal blood mainly as a low molecular weight (LMW) trimer, hexamer, and a high molecular weight (HMW) multimers. Low circulating levels of adiponectin are related to metabolic syndrome. We have then investigated the influence of immobilization stress on plasma adiponectin concentrations in mice. Relative LMW and HMW adiponectin levels were markedly reduced by immobilization stress (0.66 +/- 0.07 and 0.59 +/- 0.06 after 102 h, respectively), significantly different from the control values (p<0.01 and 0.05, respectively). gamma-Aminobutyric acid (GABA) and gamma-oryzanol abundantly contained in germinated brown rice have some physiological functions. We further investigated the effect of GABA, gamma-oryzanol, GABA plus gamma-oryzanol on adiponectin levels in mice subjected to immobilization stress. GABA and gamma-oryzanol significantly increased the relative LMW and HMW adiponectin levels under immobilization stress (1.10 +/- 0.11 and 0.99 +/- 0.19 after 102 h, respectively, for GABA; 1.08 +/- 0.17 and 1.15 +/- 0.17 after 102 h, respectively, for gamma-oryzanol). Additionally, the co-administration of GABA and gamma-oryzanol also increased both relative LMW and HMW adiponectin levels (1.02 +/- 0.07 and 0.99 +/- 0.10 after 102 h, respectively) and was effective in an earlier phase from 30 to 54 h. The results indicate that the co-administration of GABA and gamma-oryzanol might be effective in preventing stress-induced hypoadiponectinemia in mice and be also a promising tool for improving metabolic syndrome aggravated by chronic stress. (C) 2011 Elsevier GmbH. All rights reserved.
Gamma-aminobutyric acid (GABA)				ENGLISH	Journal	Alternative Medicine Review; ALTERN. MED. REV.	
Oral gabapentin premedication for elderly patients undergoing intraocular surgery.	Kavitha, J	Parida, Satyen; Kundra, Pankaj; Srinivasan, Renuka	2013 Jul	English	Comparative Study; Journal Article; Randomized Controlled Trial	Br J Ophthalmol	To compare effects of gabapentin premedication with diazepam in patients undergoing cataract surgery. In a randomised double-blind study, the effects of gabapentin premedication as a sedative, anxiolytic, analgesic and oculohypotensive agent were studied in 56 elderly patients undergoing elective intraocular surgery. There was significantly more sedation in the diazepam group than in the gabapentin group. However, there was less subjective anxiety in the gabapentin group than in the control group. There was a significant fall in intraocular pressure (IOP) and significant reduction in mean arterial pressure in the gabapentin group compared with the control group. Perioperatively, significantly more supplementation with intravenous midazolam was given in the control group than in the gabapentin group. A significantly larger number of patients in the gabapentin group scored a postanaesthesia recovery score of 10 compared with the control group. There was a statistically significant difference in the postoperative visual analogue scale scores for pain and number of analgesic requests with gabapentin scoring over diazepam in this regard. Hence, premedication with oral gabapentin in these elderly patients undergoing elective intraocular surgery produced intraoperative anxiolysis, decreased sedation, a modest decrease in IOPs and improved postoperative recovery.

Valeriana officinalis root extracts have potent anxiolytic effects in laboratory rats.	Murphy, K.	Kubin, Z. J.; Shepherd, J. N.; Ettinger, R. H.	2010-07	English	Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.	Phytomedicine	Valerian root ( <i>Valeriana officinalis</i> ) is a popular and widely available herbal supplement, primarily used to treat insomnia and anxiety. Until recently, its mechanism of action has remained unknown. Neurobiological research has begun to show that the herb, with its active valerenic acid, interacts with the GABA(A)-ergic system, a mechanism of action similar to the benzodiazepine drugs. This series of experiments sought to corroborate these findings with behavioral measures, compare them to the benzodiazepine diazepam, and to analyze the chemical composition of <i>Valeriana officinalis</i> . Rats were administered either ethanol (1 ml/kg), diazepam (1mg/kg), valerian root extract (3 ml/kg), valerenic acid (3mg/kg), or a solution of valerenic acid and exogenous GABA (75 microg/kg and 3.6 microg/kg, respectively) and assessed for the number of entries and time spent on the open arms of an elevated plus maze. Results showed that there was a significant reduction in anxious behavior when valerian extract or valerenic acid exposed subjects were compared to the ethanol control group. The evidence supports <i>Valeriana officinalis</i> as a potential alternative to the traditional anxiolytics as measured by the elevated plus maze.
Anti-hypertensive effect of gamma-aminobutyric acid (GABA)-rich Chlorella on high-normal blood pressure and borderline hypertension in placebo-controlled double blind study.	Shimada, Morio	Hasegawa, Takashi; Nishimura, Chiaki; Kan, Hiroko; Kanno, Toshihiro; Nakamura, Toshio; Matsubayashi, Tsuneo	2009-06	English	Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't	Clin Exp Hypertens	The anti-hypertensive effect of GABA-rich Chlorella was studied after oral administration for 12 weeks in the subjects with high-normal blood pressure and borderline hypertension in the placebo-controlled, double-blind manner in order to investigate if GABA-rich Chlorella, a dietary supplement, is useful in control of blood pressure. Eighty subjects with Systolic blood pressure (SBP) 130-159 mmHg or diastolic blood pressure (DBP) 85-99 mmHg (40 subjects/group) took the blinded substance of GABA-rich Chlorella (20 mg as gamma-aminobutyric acid) or placebo twice daily for 12 weeks, and had follow-up observation for an additional 4 weeks. Systolic blood pressure in the subjects given GABA-rich Chlorella significantly decreased compared with placebo ( $p < 0.01$ ). Diastolic blood pressure had the tendency to decrease after intake of GABA-rich Chlorella. Neither adverse events nor abnormal laboratory findings were reported throughout the study period. Reduction of SBP in the subjects with borderline hypertension was higher than those in the subjects with high-normal blood pressure. These results suggest that GABA-rich Chlorella significantly decreased high-normal blood pressure and borderline hypertension, and is a beneficial dietary supplement for prevention of the development of hypertension.
Role of the renal nerves in gamma-aminobutyric acid-induced antihypertensive effect in spontaneously hypertensive rats	Hayakawa, Kazuhito	Kimura, Masayuki; Yamori, Yukio	NOV 7 2005	English	Article	European Journal of Pharmacology	The aim of this study was to clarify the role of the renal sympathetic nerves in the gamma-aminobutyric acid (GABA)-induced hypotensive effect in spontaneously hypertensive rats. Male spontaneously hypertensive rats (SHR/Izm) aged 7 weeks were divided into four groups on the basis of diet (containing 0.05% GABA, or GABA-free control diet) and operation (renal sympathetic-denervated or sham-operated) (n=10, each). Water intake, urine volume and urinary sodium were, or tended to be, slightly higher, while plasma renin activity was significantly lower in the GABA group than the GABA-free control group. GABA inhibited the development of hypertension in sham-operated spontaneously hypertensive rats but not in renal-denervated spontaneously hypertensive rats. Plasma renin activity was significantly higher in sham-operated spontaneously hypertensive rats fed the control diet than in the other three groups. These results suggest that a reduction in the effects induced by the renal nerves may play an important role in the hypotensive effect induced in spontaneously hypertensive rats by chronic dietary administration of GABA. (c) 2005 Elsevier B.V All rights reserved.
Formulations of dietary supplements and herbal extracts for relaxation and anxiolytic action: Relarian.	Weeks, Benjamin S.		2009-11	English	Journal Article; Review	Med Sci Monit	Dietary supplements are widely used for desired effects on memory, insomnia, mood and anxiety. This review focuses on supplements which have anxiolytic or mild relaxation properties and enhance mood. For example, Kava ( <i>Piper methysticum</i> ) is reported to have anxiolytic actions and to reduce tension through skeletal muscle relaxation. Dried passion flower (genus <i>Passiflora</i> ) is reported to reduce insomnia and hysteria. Skullcap (genus <i>Scutellaria</i> ), hops ( <i>Humulus lupulus</i> ), lemon balm ( <i>Melissa officinalis</i> ) and Valerian ( <i>Valeriana officinalis</i> ) root are all herbs reported as anxiolytic calming agents. Further, extracts of Magnolia and Phellodendron bark are mild sedatives. Supplements such as gamma-aminobutyric acid (GABA), theanine, tryptophan and 5-hydroxytryptophan (5-HTP) are reported to promote relaxation. In general, these supplements appear to act as GABA receptor agonists or to boost GABA levels, although Kava inhibits both norepinephrine uptake and sodium and potassium channels and 5-HTP may act through elevation of serotonin. While questions remain in the literature regarding the medicinal value of these supplements in treating mood and anxiety disorders, based on cellular and animal studies as well as human clinical trials the literature supports a role for these preparations as useful alternatives in the management of the stress and anxiety of everyday life.