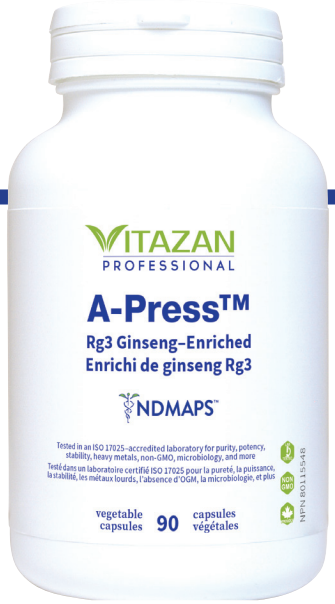
VITAZAN PROFESSIONAL

A-Press™

Rg_3 Ginseng–Enriched



An Rg_3-Ginseng Specific Product

Ginsenoside Rg_3 from ginseng—the most potent anticancer metabolite in *Panax ginseng*—requires biotransformation of the intestinal microbiome, making the effects from this molecule dependent on host microbiota.[1] These metabolites have been demonstrated to exert antiangiogenic effects, particularly in pulmonary, gastric, and ovarian cancers.[2] Rg_3 has been demonstrated to inhibit NF-κB signalling.[3] The antiangiogenic effects from Rg_3 may also be due to the downregulation in the expression of vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR), and by targeting hypoxia-induced signalling pathways, among many other possible pathways.[4][5][6] Rg_3 has antitumour effects via reducing insulin growth factor (IGF) and by inhibiting aquaporin-1 (AQP-1).[7][8] Both enantiomers—R and S—for Rg_3 have effects in different cancer cell lines, and so we have chosen to include both in our product.[9]

One preclinical trial in a breast-cancer tumour model in mice demonstrated that Rg_3 in combination with capecitabine—a prodrug of fluorouracil—decreased toxicity of the chemotherapeutic, produced a longer survival, and created less drug resistance.

There are four published human clinical trials on the use of Rg_3 ginsenosides in cancer: Three in non–small-cell lung cancer (NSCLC), and one on hepatocellular carcinoma (HCC).[10][11][12][13]

In a study of 124 patients with advanced NSCLC and the EGFR mutation, subjects were treated with standard therapy alone ($n = 72$) or in conjunction with Rg_3 ginsenoside ($n = 52$).[14] After 22.9 months, progressive free survival time was significantly longer in the combined group versus the standard group, as was the objective response rate. The overall survival rate was no different between the two groups.[15]

In a prospective randomized control trial, 133 patients with stage II–III NSCLC received either Rg_3 ($n = 43$), Rg_3 with chemotherapy ($n = 46$), or chemotherapy alone ($n = 44$). Rg_3 with chemotherapy improved the three-year survival rate by 54.3%, compared to 46.5% in the Rg_3 group and 47.7% in the chemotherapy group. The improvement was attributed to a more balanced immune system via a favourable ratio of CD4/CD8, while the groups without Rg_3 had a disproportionate ratio.[16]

In a single, open-label, randomized controlled trial, 228 patients with advanced hepatocellular carcinoma were to receive either transcatheter arterial chemoembolization (TACE) alone ($n = 76$) or in conjunction with Rg_3 ginsenosides ($n = 152$). Primary endpoint of overall survival was statistically greater in the combined group (13.2 months versus 10.1 months, $p = 0.002$). Disease control rate was also statistically better in the combined group, and Rg_3 appeared to have alleviated some TACE adverse events and blood anomalies.[17]

A randomized, placebo-controlled, double-blind trial involving 414 patients with III–IV non–small-cell lung cancer investigated the effect of first-line

chemotherapy combined with ginseng Rg_3 (n = 199), versus the same chemotherapy combined with placebo (n = 215). The median overall survival was significantly better in the treatment group v. the placebo group (12.03 v. 8.46 months, respectively [$p < 0.05$]). While hemoglobin and white blood cells were decreased in both groups, those adverse events were significantly milder in the treatment group ($p < 0.05$). The authors conclude that the combined therapy improved patients' symptoms and reduced chemotherapy induced myelosuppression.[18]

Athanasios Psihogios and Dugald Seely's article "Antiangiogenic phytochemicals best poised for clinical trial testing—A literature review of the most promising natural agents for integrative oncology research" provides supporting research for the inclusion of green tea, curcumin, resveratrol, and ginsenoside included in A-Press™.[19]

Each vegetable capsule contains:

Red ginseng (*Panax ginseng*) root extract, 45% ginsenosides Rg_3 ..... 15 mg
Red ginseng (*Panax ginseng*) root extract, 20% ginsenosides..... 15 mg
Green tea (*Camellia sinensis*) leaf extract, 75% epigallocatechin-3-gallate..... 200 mg
Turmeric (*Curcuma longa*) root extract, 95% curcuminoids, providing curcumin I, demethoxycurcumin, and bisdemethoxycurcumin ..... 200 mg
Bromelain (from pineapple [*Ananas comosus* var. *comosus*] stem), 2,400 GDU/g (3,600,000 FCC papain units) ..... 50 mg
Japanese knotweed (*Fallopia japonica*) root, 50% *trans*-resveratrol ..... 30 mg

Suggested use: Take 1 capsule twice daily or as directed by your health-care provider. Please consult your health-care practitioner or naturopathic doctor for use greater than 1 month.

Cautions and warnings: Discontinue use and consult a health-care practitioner if you develop symptoms of liver trouble, such as yellowing of the skin/eyes (jaundice), stomach pain, dark urine, sweating, nausea, unusual tiredness, or loss of appetite; if you are pregnant or breast-feeding; if you have gallstones, a bile duct obstruction, stomach ulcers, or excess stomach acid; if you are taking prescription medications, as resveratrol may alter their effectiveness; or if symptoms persist or worsen.

Contraindications: For use in proximity to surgery and during wound healing.

Known adverse reactions: Rare, unpredictable cases of liver injury associated with green tea extract–containing products have been reported (in Canada and internationally). Discontinue use if hypersensitivity/allergy occurs. May cause nausea, abdominal pain, and/or diarrhea.

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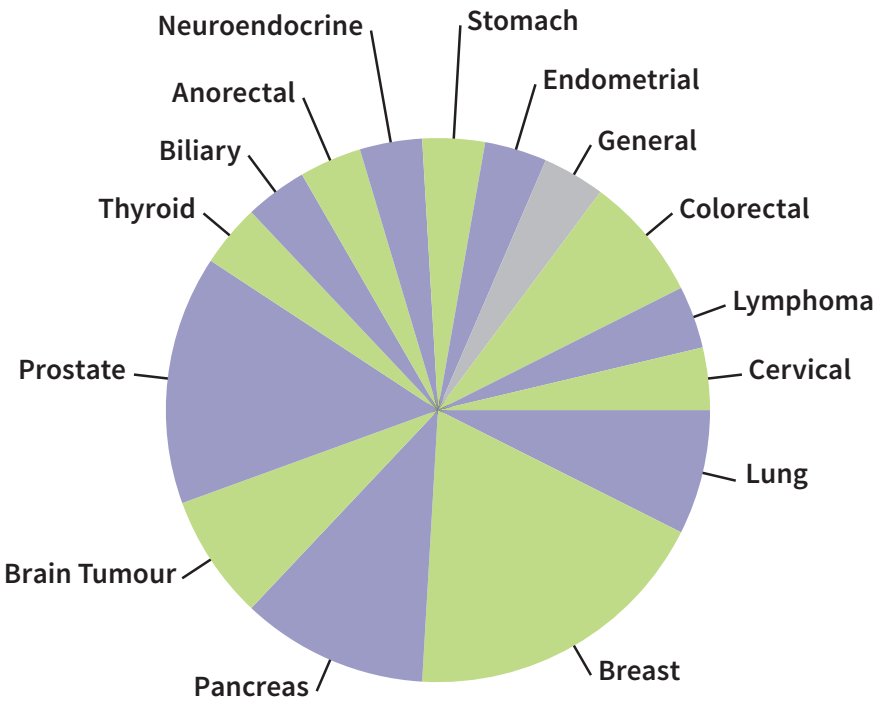
The following graphs are summaries of the surveillance data collected by naturopathic doctors in the Medical Advancement Panel on the use of their product formulations in practice.



Lung:	2
Breast:	5
Pancreatic:	3
Brain Tumour:	2
Prostate:	4
Thyroid:	1
Billiary:	1
Anorectal:	1
Neuroendocrine:	1
Stomach:	1
Endometrial:	1
General:	1
Colorectal:	2
Lymphoma:	1
Cervical:	1
Total:	**27**

Figure 1: A-Press™—Number of Cases per Cancer Type
(March 2021—November 2021)

This graph shows the number of cases that are being followed, and the distribution of cancer types. There were a total of 27 cases.

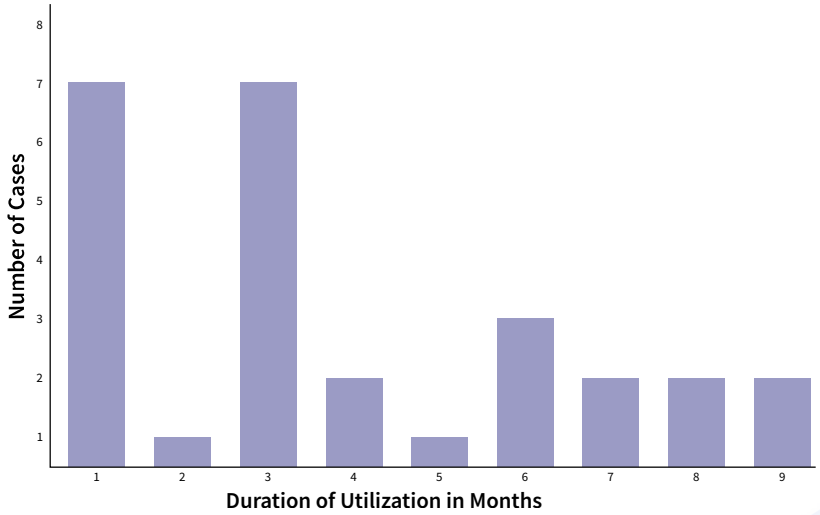


Figure 2: A-Press™—Number of Cases per Duration of Utilization
(March 2021—November 2021)

This graph demonstrates the distribution of duration of utilization. Note that of these cases, a certain proportion are still receiving ongoing treatment.

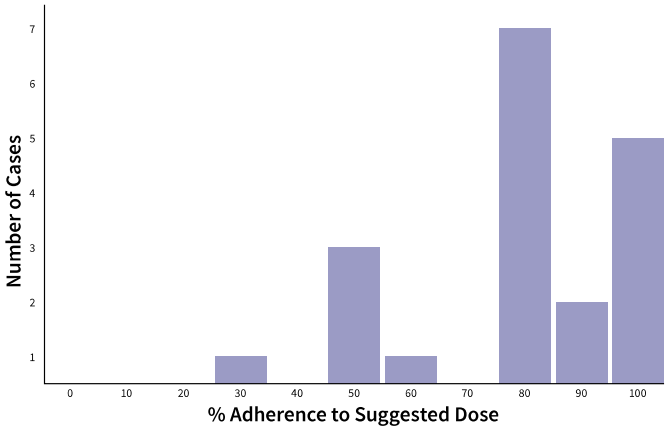


Figure 3: A-Press™—Adherence to Suggested Dose

This graph depicts the number of cases who followed the prescribed regimen, providing insight on tolerability and easy of compliance.

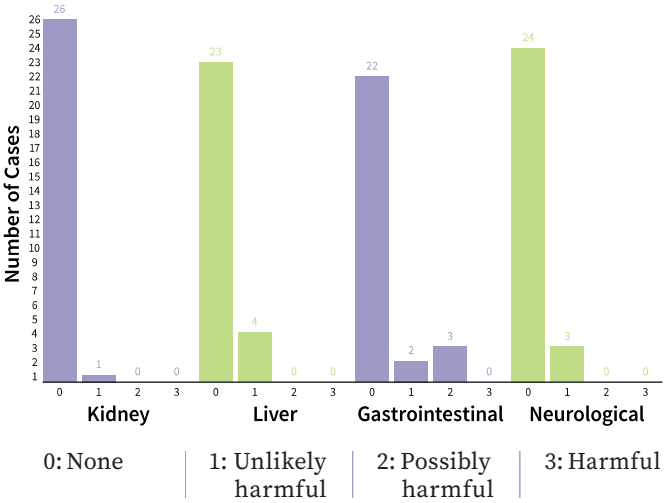


Figure 4: A-Press™—Side-Effect Profile

This graph shows the number of cases that experienced a worsening in organ function versus the likelihood that it was caused by the treatment. Cases have some preexisting degree of organ dysfunction due to disease or chemotherapy.

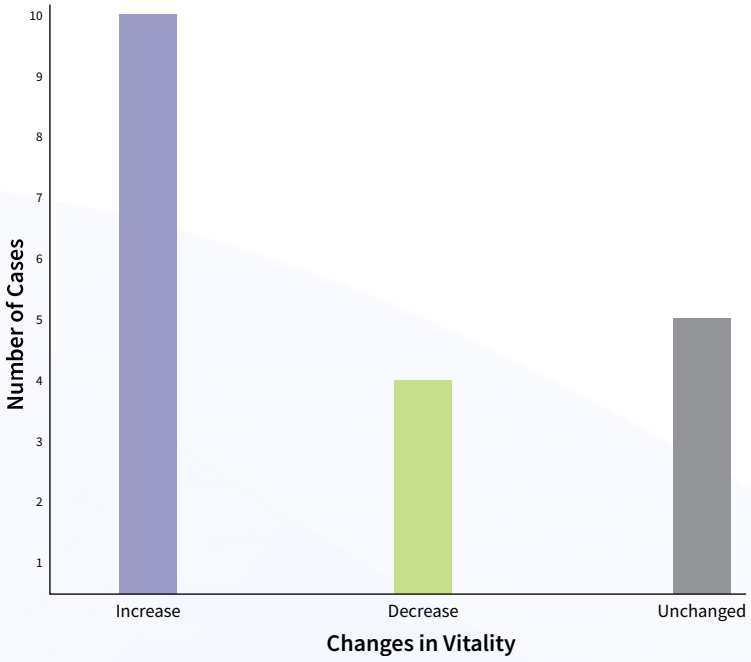


Figure 5: A-Press™—Vitality Evolution

This graph demonstrates the subjective observation in overall vitality as assessed.