AIBMR Life Sciences

The Discovery of a Novel Immune Modulatory Agent: EpiCor

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High Metabolite Immunogens

EPICOR™

Birth of EpiCor

- A midwest farmer in Iowa created a fermentation product from a commonly consumed yeast that unexpectedly caused animals to be exceptionally healthy.
- This product has been produced for over 60 years and is now included in animal feed products sold world-wide.

Birth of EpiCor (I)

•An unusually low incidence of health problems and use of sick leave was discovered among a group of employees working at a fermentation plant in Cedar Rapids, Iowa.

•The discovery was made when the company became self-insured. Year-to-year health care expenditures defied actuarial/underwriter estimates of how much money the company needed to set aside to cover anticipated health care expenditures for its employees.

Birth of EpiCor (II)

Reduction in time lost due to illness improved the company's profitability and turnover.

- With minimal increases in health premiums each year, amounting to an enviable 0-3% per year increase, extraordinarily low for companies in America, the company was able to reduce cash demands for their self-insurance fund.

- The possibility that the ingredient the employees were handling in the production facility might explain the unusually low rate of illness among employees at the production facility, led to the request to have AIBMR Life Sciences visit the facility and an open ended investigation of the ingredient's composition.

Human Blood Study of "Exposed and Non-exposed" Employees

METHODS:

- Two groups of subjects: one group (n=10) consisted of production employees "exposed" to EpiCor, working in the fermentation plant, and a "non-exposed" group (n=10, control), gender/age matched control group, working in non-production positions for the same company and in the same city.
- Blood samples were used to analyze each subject's lymphocyte sub-populations, red blood cell total glutathione, and an extensive auto-immune panel, which together looked at over 50 immune parameters. Saliva samples were also collected to determine secretory immunoglobulin A (IgA) levels.

HIGHLIGHT OF RESULTS:

Compared to the control, the exposed group showed a:

1) significant decrease in CD8 (suppressor cells) number resulting in a significantly higher CD4 (helper cells) to CD8 cell ratio ($p<0.01$);
2) significantly higher cytotoxic activity of natural killer (NK) cells despite a significant decrease in the number of NK cells ($p<0.01$);
3) significantly higher levels of total salivary secretory IgA ($p<0.01$)(non-exposed:182.1 m g/mL, mean 20.2 vs. exposed: 305.8 mg/mL, mean 34.0);
4) significantly lower levels of immune complexes ($p<0.01$);

Human Blood Study(continued)

RESULTS (continued):

- a significantly higher levels of specific antibodies ($p<0.01$) (182.9 mg/mL, mean 20.3 vs. 243.9 mg/mL, mean 27.3);
- a higher killing efficiency of NK cells (12.4% vs. 15.1%); and,
- a higher level of glutathione in erythrocytes (721 vs. 756 mM).

CONCLUSIONS:

- Exposure to EpiCor resulted in an enhanced adaptive immune response and improved NK cell cytotoxic activity;
- Lower levels of immune complexes in the exposed individuals may be responsible for less inflammation, and hence result in less tissue damage, associated with aging; and,
- The exposed group has an optimally functioning innate (humoral) immune system. (Innate immunity is the non-specific part of immunity and the generalized response the body has to the presence of an invader.)

LABORATORY: Immunosciences Laboratory Inc., Beverly Hills, CA

Does EpiCor Have Antioxidant Activity?

Oxygen Radical Absorbance Capacity (ORAC) Assays (ORAC)

Among foods, cranberries has the highest reported antioxidant activity at 92.55 μmole TE/g (dry weight), according to published 2005 USDA data; blueberries is ~ 62 μmole TE/g.

RESULTS for EpiCor:

Total ORAC	(peroxyl radical)	614 μmole TE/g (+/-15%)
NORAC	(peroxynitrite radical)	54 μmole TE/g
HORAC	(hydroxyl radical)	214 μmole CAE/g
SOD	(superoxide anion)	2.2 kU SOD eq/g

CONCLUSION:

The Total (hydrophilic and lipophilic) ORAC activity of EpiCor against peroxyl free radicals is higher than that of blueberries or other antioxidant rich foods per gram (Wu, X et al. *J Agricul Food Chem*, 2005).

ORAC info: Bank G, Schauss A. Antioxidant testing: An ORAC update. Nutraceuticals World, 2004; 7(3): 68-71.

LABORATORY: Brunswick Laboratories, Wareham, MA. Total ORAC confirmed at USDA Lab.

Does EpiCor Inhibit Radical Oxygen Species (Free Radicals) Formation in Human Blood?

METHOD:

Freshly purified human cells (neutrophils) are incubated with aliquots of diluted EpiCor and then exposed to a dye that can make radical oxygen species (free radicals) be seen by researchers.

The colorless dye is able to penetrate the cells and, after exposure to free oxygen radicals, undergoes a transformation to a fluorescent molecule that is retained inside the cells, and can be measured.

All samples are challenged with hydrogen peroxide (H_2O_2) a ROS able to induce severe oxidative stress, as is possible in the body.

- Controls consist of untreated cells and those treated with H_2O_2 in the absence of the extract.
- Intracellular levels of the fluorescence intensity are measured and compared between untreated vs. challenged cells in the presence or absence of the extract.

Inhibition of ROS Formation

RESULTS:

- Treatment with 10 ppm, 100 ppb, 1 ppb and 1 ppt dilutions of EpiCor resulted in a significant (41-82%) reduction of ROS formation compared to the control cells challenged with H2O2 in the absence of the extract.
- EpiCor at 1 part per trillion (ppt) resulted in a significantly lower fluorescence intensity than that of the untreated cells.
- It only became ineffective in ROS inhibition when EpiCor was diluted down to < 0.01 ppt.

CONCLUSION:

The results indicate that EpiCor is most effective in inhibiting ROS formation at 1 ppt - the physiologic level of cellular metabolism. Such an extremely low concentration may allow a better penetration of EpiCor compounds beneficial to the human immune system inside of cells.

LABORATORY: NIS Labs, Klamath Falls, OR

What is the Composition of EpiCor?

Macronutrients

RESULTS (Fractionation Analysis):

	g/100 g	mg/500 mg
Moisture	12.5	62.5
Protein	30.0	150.0
Carbohydrate	11.2	56.0
Ash	19.1	95.5
Lipid extract	5.8	29.0
Insoluble fiber	16.3	81.5
Soluble fiber	13.8	69.0
Total fiber	30.1	150.5
β-Glucan	5.5	27.4
Miristic (C14)	0.1	0.38
Palmitoleic (C16:1)	0.5	2.61
Palmitic (C16)	2.2	10.89
Oleic (C18:1)	0.1	0.47
Stearic (C18)	0.5	2.25

Found to contain both beta-glucans and other glucans and mannan oligosaccharides, not found in yeast extracts.

LABORATORY: V-Labs, Inc., Covington LA

Micronutrients: Vitamins

RESULTS: Vitamins	mg/100 g	mg/500 mg
Thiamin (vitamin B1)	1.5	0.008
Riboflavin (vitamin B2)	0.9	0.005
Niacin (vitamin B3)	1.4	0.002
Pantothenic acid	0.3	0.013
Pyridoxin (vitamin B6)	2.5	<0.001
Cobalamin (vit. B12)	0.01	<0.001
Folic acid	0.01	<0.001
Biotin	<0.01	<0.001

Full complement of B-vitamins at varying concentrations.

LABORATORY: IBC Labs, Tucson, AZ

Micronutrients: Minerals

RESULTS: Minerals	g/100 g	mg/500 mg
Calcium	0.92	4.60
Magnesium	0.81	4.05
Sodium	0.17	0.85
Potassium	7.20	36.00
Phosphorus	1.30	6.50
Sulfur	1.40	7.00
Zinc	0.01	0.05
Iron	0.03	0.15
Copper	0.001	0.01
Manganese	0.003	0.015
Selenium	nd	nd
Lead levels were extremely low at	<0.0001	<0.0005

LABORATORY: V-Labs, Inc., Covington LA

Phytosterols

RESULTS:

	mg/100 g	µg/500 mg
Squalene	0.35	1.73
Zymosterol	0.2	1.03
Ergosterol	12.29	62.45
Fecosterol	0.27	1.33
Episterol	0.51	2.54
Lanosterol	1.13	5.64

Ergosterol is the biological precursor to vitamin D-2. It is turned into viosterol by ultraviolet light, and is then converted into ergocalciferol, which is a form of Vitamin D.

Squalene is manufactured in the liver and found abundantly in human skin and considered the skin's natural antioxidant. The source of squalene in dietary supplements usually comes from certain species of shark.

LABORATORY: IBC Labs, Tucson, AZ

Phenolics

RESULTS:

	g/100g	mg/500 mg
Catechin	2.95	14.75
Pyrogallol	1.73	8.65
Resourcinol	0.79	3.95
Trans-resveratrol	0.72	3.60
Vanillic alcohol	0.65	3.25
Cresol	0.60	3.00
Guaiacol	0.43	2.15
Total phenolics:	9.43	47.15

Catechins are bioflavonoids, polyphenols and powerful anti-oxidants. Sources of catechins are white tea and green tea. Catechins are linked to evidence in enhancing immune system function due to their polyphenol antioxidant character, which is well established in scavenging reactive oxygen species (ROS).

LABORATORY: IBC Labs, Tucson, AZ

Is EpiCor Safe To Ingest by Humans?

In Vitro and *In Vivo* Toxicity/Safety Studies

Anti-Microbial Test

ANALYSIS: To determine the effect of EpiCor on growth of three pathogenic bacteria (*Staphylococcus aureus*, *Escherichia coli),* and the fungi (*Candida tropicalis*) and on normal oral bacteria, using well known *in vitro* test.

RESULTS:

- EpiCor significantly reduced the growth of *E. coli* and *C. tropicalis* at dilutions down to 1 ppt, but only marginally of *S. aureus* above 1 ppm.

CONCLUSION:

Consumption of EpiCor may provide protection against infection of coliform bacteria and *Candida*. Thus, it may support the growth of desirable mucosal flora, and have an important prebiotic effect that would help keep intestinal bacteria within more optimal levels, allowing desirable bacteria to provide needed secondary metabolites that are absorbed into blood and contribute to human health.

LABORATORY: NIS Laboratory, Klamath Falls, OR

Stability Tests

TEST 1: EpiCor kept at room temperature without inoculation.
During 38 days, levels of mold, *Salmonella*, and *Staphylococcus aureus* stayed below the acceptable level of 10 cfu/g.

TEST 2: EpiCor was inoculated with yeast, mold, lactic acid, *Salmonella*, and *S. aureus* and kept at room temperature for 28 days.
Levels of mold, *Salmonella* and *S. aureus* decreased, whereas those of yeast and lactic acid increased, which was as expected because of the nature of the product.

TEST 3: Real time shelf-life stability of EpiCor for 23 months at ambient temperature (73-77 F [25 C]) and humidity, with monthly analyses of aerobic bacteria, lactic acid bacteria, yeast, and mold, supports a two year shelf-life.

Result: EpiCor has a microbiological shelf-life of two yeas when stored at proper room temperature and humidity.

LABORATORY: Silliker Laboratory Inc., Research Center, Holland, IL

Pesticide Assay

OBJECTIVE: To verify the presence of three classes of pesticides (organo-phosphate, organo-nitrogen, and organo-chloride), n--methyl carbamates, ethyl-bis-thiocarbamates (EBDC's), and piperonyl butoxide in EPICOR.

METHOD: The presence of 139 analytes were assessed using the Luke OP/ON, Luke OC, Luke CB, and EBDC screening panels, following FDA 302 extraction method for the first three, CDFA extraction method for the fourth group, and a specific method for piperonyl butoxide.

RESULTS: Based on the method of extractions used in the analyses, EpiCor was found free of all 139 pesticides and compounds tested at the lowest possible detection limits.

LABORATORY: Environmental MicroAnalysis, Inc., Woodland, CA

Acute 14-Day Oral Toxicity Study (Limit Test)

STUDY DESIGN:

Rats (n = 20) were force-fed by gavage an acute dose of 2,000 mg EpiCor/kg of body weight (equal to approximately 140 grams taken at one time = 280 capsules, by an adult) on day one, then observed for consecutive 14 days for any side effects, then euthanized according to strict animal review board requirements, on day 15, and then examined by qualified animal toxicologists.

RESULTS:

- No death occurred;
- Normal body weight and body weight gain;
- No toxic clinical symptoms; and,
- No gross pathological changes or lesions were found.

CONCLUSIONS:

These results indicate that EpiCor is not toxic at extremely high doses in this mammalian species.

LABORATORY: PDC Laboratory, Budapest, Hungary

Subchronic 90-Day Oral Toxicity Study

METHOD:

Four groups of rats (number = 40 per group; 20 males, 20 females in each cohort), was force-fed by gavage either 30, 200 or 1,500 mg EpiCor/kg of body weight for 90 consecutive days or not force-fed (control). 90 days is allometrically equivalent to 1.5 human years of life.

RESULTS:

The treated rats given EpiCor showed:

- no mortality and no treatment related clinical symptoms
- no significant differences in body weight and food and water consumption compared to the control
- no pathological changes in the eyes
- no change in sensory reactivity, grip strength and motor activity
- no change in hematological parameters or prothrombin time.
- no change in serum and urine metabolic parameters
- no gross pathological lesions in the organs of the digestive, respiratory, circulatory, urinary, endocrine, reproductive, nervous (central and peripheral), and lymphoid systems.

Subacute 90-Day Oral Toxicity Study (continued)

CONCLUSIONS:

- The results indicate that the test product was well tolerated in daily oral doses up to 1500 mg/kg of body weight.
- The “no observed adverse effect level” (NOAEL) in rats is higher than 1500 mg/kg consumed for 90 days”, according to the toxicologists who performed this extensive study.

  NOTE: Allometrically such a dose is equivalent to 105 grams (210 capsules a day) of EpiCor taken every day for ~1.5 years by a 70-kg adult male or 50-kg adult female.

The acute and subchronic toxicity studies were done according to GLP, OECD, EU, and US FDA compliance standards, by a leading toxicology lab with over 50 years of experience in toxicology.

LABORATORY: PDC Laboratory, Budapest, Hungary

Bacterial Reverse Mutagenicity Test
(AMES Test)

METHOD:

- EpiCor was evaluated in a bacterial reverse mutation assay employing *Salmonella typhimirium* (strains TA97a, TA98, TA100, TA1535) along with *Escherchia coli* (strain WP2 *uvr,* A328) both in the presence and absence of an exogenous metabolic activation system.
- Concentrations of 10, 50, 100, 500, and 1000 μg of EpiCor/plate were assessed with respect to negative (solvent) controls in the confirmatory pre-incubation assay.

RESULTS:

No evidence of mutagenic activity was detected for EpiCor in the tested strains of *S. typhimirium* and *E.coli*.

CONCLUSION:

The results indicate a negative mutagenic effect of EpiCor under the conditions of the bacterial reverse mutation test.

LABORATORY: Next Century Inc., Newark, DE

Mouse Lymphoma L5178Y Cell Mutagenicity Assay

OBJECTIVE: to verify the genotoxic potential EpiCor by using the mammalian cell mutation assay system that detects mutations at the thymidine kinase (TK) locus of lymphoma L5178 cells.

METHODS:

- Two independent trials, each trial consisting of two experiments are conducted either with or without metabolic activation.
- In the experiments in the presence of metabolic activation, mouse lymphoma L5178Y cells are exposed for 3 hours to 625, 1250, 2500 or 5000 μg of the test product/mL of incubation medium containing post-mitochondrial supernatant of the liver of rats treated with Aroclor 1254.
- In Trial 1 for the experiment in the absence of metabolic activation, Mouse Lymphoma L5178Y cells are exposed to the test product at each concentration for 3 hours, whereas in the confirmatory Trial 2 for 24 hours continuously.
- In a similar way, concurrent negative controls and appropriate positive controls were tested viz., cyclophosphamide in the presence of metabolic activation and methylmethane sulphonate in the absence of metabolic activation.

Mouse Lymphoma L5178Y Cell Mutagenicity Assay(continued)

RESULTS:

- There was no evidence of induction of gene mutation by EpiCor in any of the experiments.
- The respective control treatments produced a significantly higher increases in the frequency of mutants under identical conditions.

CONCLUSION:

The results indicate that EpiCor is not mutagenic as it does not have the potential to cause gene mutation at the TK locus at the concentrations tested and under the conditions of testing.

LABORATORY: Rallis Research Centre, Bangalore, India

Immortalized Hepatocyte Assay

Approximately 42% of the US adult population is on medication.

GOAL: To evaluate the potential of EpiCor to effect hepatocytes and induce the activity of drug-metabolizing enzymes such as cytochrome P450 1A2 (CYP1A2) and 3A4 (CY P3A4) in immortalized human hepatocytes (Fa2N-4) cells

METHOD:

- The Fa2N-4 cells are treated with either EpiCor (either concentrations ranging from 0.02 to 33.7 μg/mL DMSO), DMSO (negative control) or omeprazole and rifampin (positive controls).
- Activity of each CYP enzyme is determined using specific reactions.
- Toxic effect is evaluated based on lactate dehydrogenease (LDH) release and light microscopic observations of the cells.
- The ability to interfere with drug metabolism is evaluated by measuring expression (mRNA) and activity of CYP1A2 and CYP3A4 in the presence of omeprazole and rifampin.

Immortalized Hepatocyte Assay (continued)

RESULTS:

Compared to the controls, EpiCor:

- was not toxic to Fa2N-4 cells
- did not induce the expression (mRNA) or enzymatic activity of CYP1A2 and CYP3A4
- did not interfere in drug metabolism by CYP1A2 and CYP3A4

CONCLUSION:

The results clearly indicate that the test product is not toxic to human hepatocytes and does not have cytochrome P450 enzyme-inducing potential.

LABORATORY: XenoTech, LLC., Lenexa, KS

An-Open-Label, Single-Dose Phase I One Month Pharmacokinetic Study

OBJECTIVE: To assess the influence of oral ingestion of 500 mg per day of EpiCor on the activity of cytocherome P450 (CYP) 3A4 and CYP2D6 and on mucosal and cell-mediated immunity in healthy adults

METHOD:

- Subjects (*n*=15, men and women aged 18-40) meeting all entry criteria received 500 mg of the test product in a single daily dose for 30 days.
- Baseline values were taken over three days preceding the experiment.
- Multiple blood samples are taken on Day-2 and again on Day 28 for pharmacokinetic profiling following administration of alprazolam (ALPZ) and dextromethorphan.
- Immune function parameters were measured in blood and saliva samples taken on Days 0, 14, 21, and 28 and sent to Immunosciences Lab.
- Vital signs and adverse events were assessed on the same days for safety monitoring.

An-Open-Label, Single-Dose Phase I One Month Pharmacokinetic Study(continued)

RESULTS:

EPICOR was well-tolerated

- Analysis of ALPZ and DX pharmacokinetics indicated that EpiCor did not affect CYP3A4 activity, nor did it significantly affect CYP2D6 activity in 12 subjects who were “extensive metabolizers” or in two subjects who were “slow metabolizers.”
- There was no evidence of any significant adverse effect of EpiCor on the immune system.
- There was no evidence of a treatment effect of EpiCor on any hematology or serum chemistry variable, nor clinically relevant changes in vital signs.
- Additional analyses is in progress.

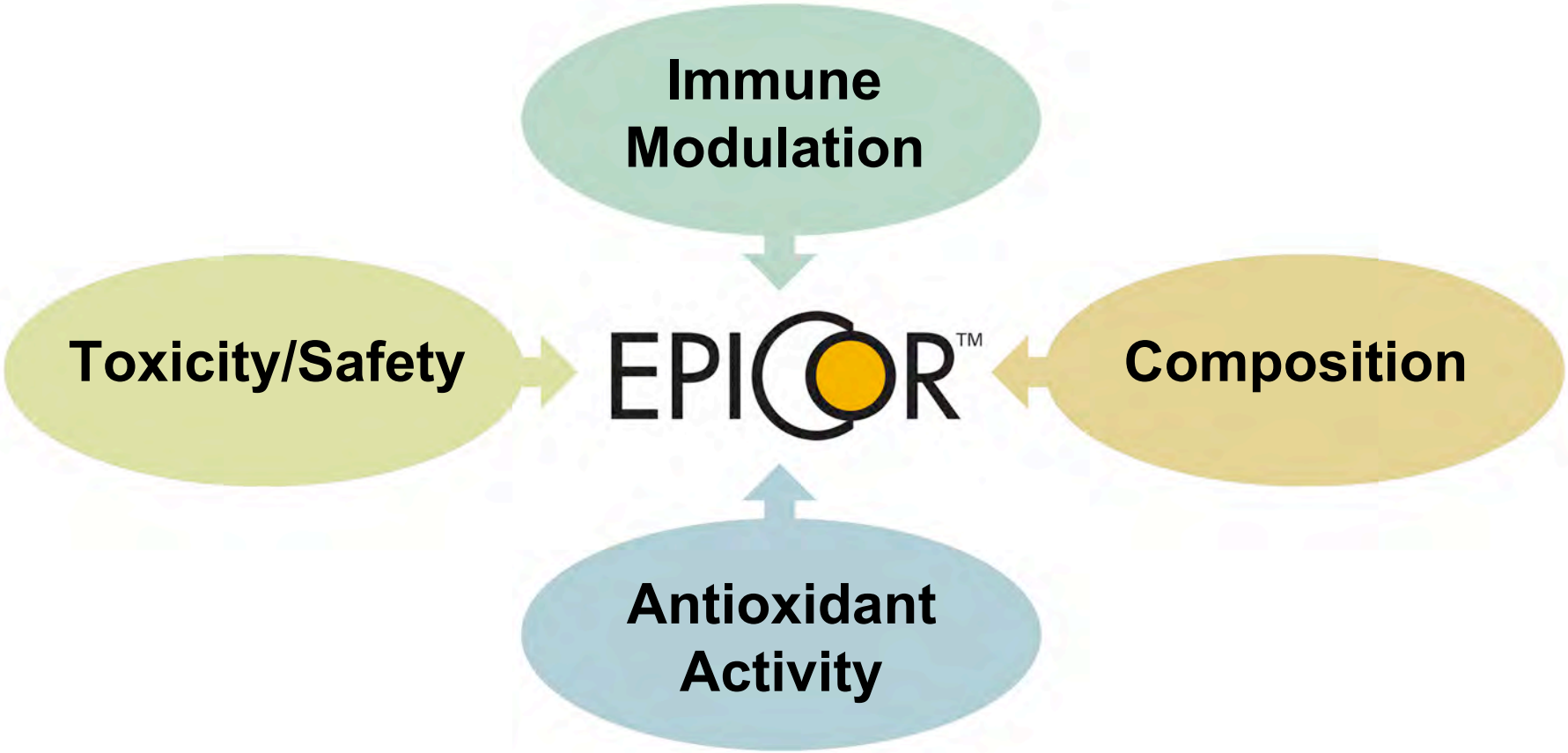
CONCLUSIONS:

- Based on the results, EpiCor posed no safety concern or clinically relevant risk with regard to hemodynamic function.
- There was no evidence of any clinically relevant effects of EpiCor on any safety parameter.

LABORATORY: Radiant Research, Inc., Chicago, IL

CONCLUSION

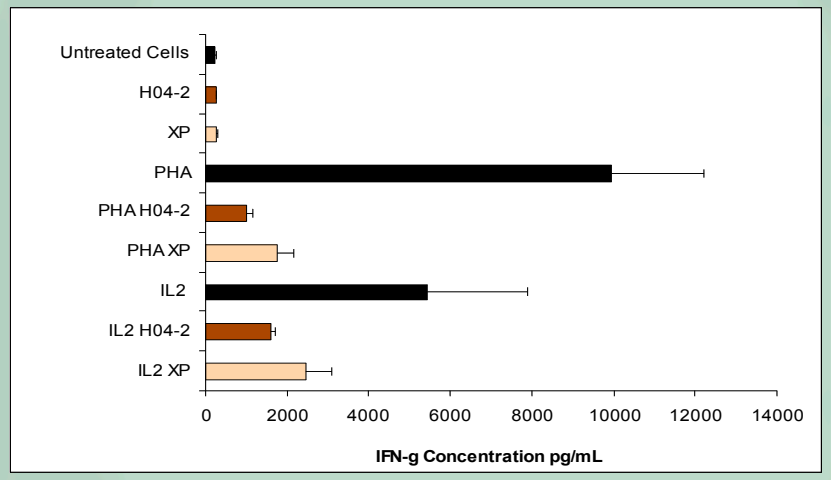
The results of all the studies completed to date indicate that EpiCor is safe, non-toxic, non-mutagenic, non-mitogenic, non-cytotoxic, and pesticide free.

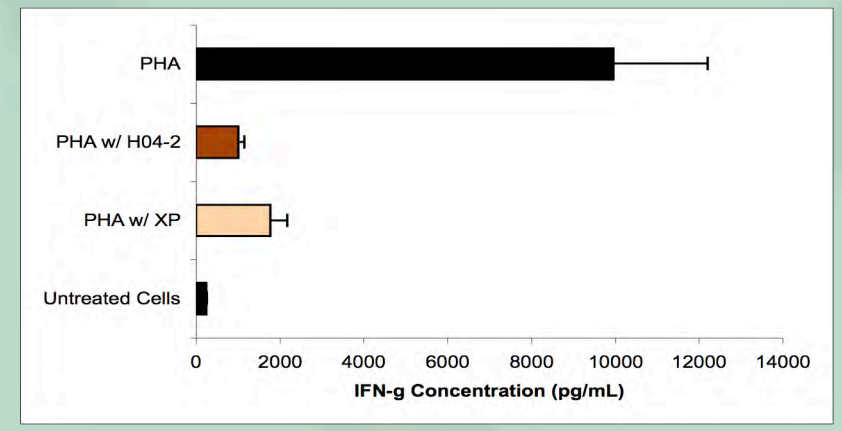

Immune Modulation
Toxicity/Safety
EPICOR™
Composition
Antioxidant Activity

Immune Modulating Effects?

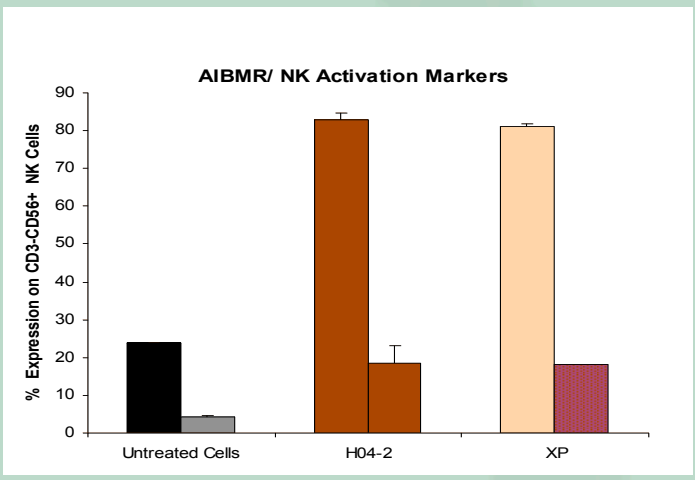
Activation of Human NK Cells *in vitro*

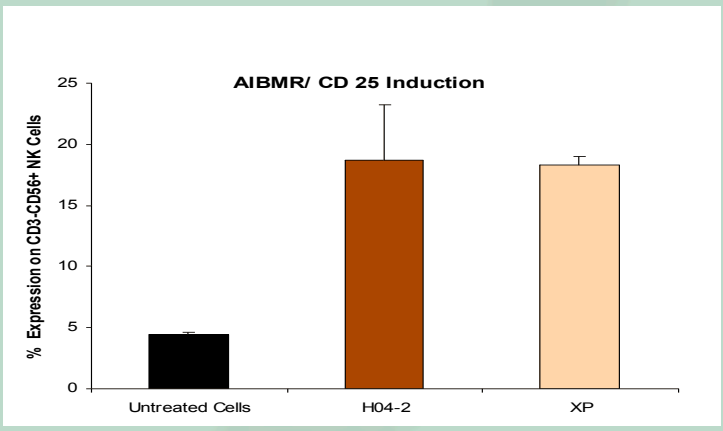
Modulation of Interferon-Gamma Production





NK Activation Markers/CD Induction





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Activation of Human NK Cells *in vitro*

RESULTS:

EpiCor appears to:

- significantly activate a majority of NK cells
- increase the ability and efficiency to kill tumor target cell lines (i.e., K562)
- significantly modulate the G-protein-linked chemokine receptor (also known as fusin or CXCR4) and the chemokine receptor-9 (CCR9) receptors on NK cells
- significantly reduce the phytohemagglutinin (PHA)-induced production of interferon-gamma
- positively modulate NK cells toward increased defense against tumor cells

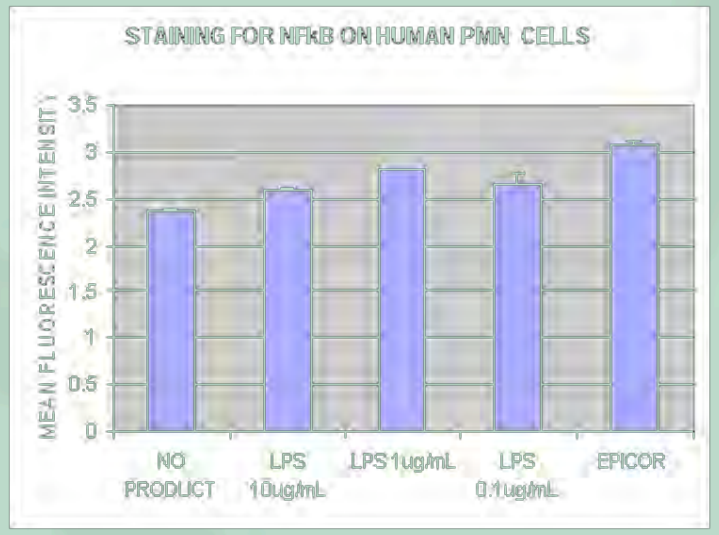
CONCLUSIONS:

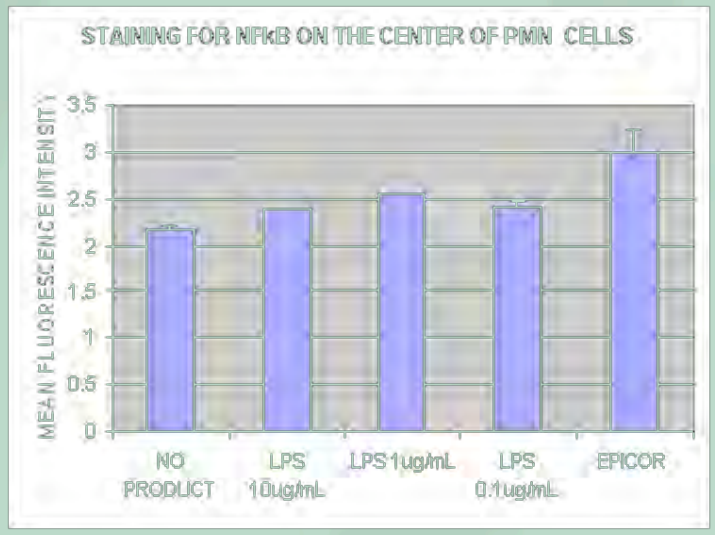
- Our body's primary defense mechanisms towards cancers and viral diseases involve a group of cells called natural killer (NK) cells. EpiCor is able to activate human NK cells and to enhance their cytotoxic capacities.
- The significant inhibition of interferon-gamma production indicates that EpiCor also has anti-inflammatory proprieties.

Eukaryotic Nuclear Factor-kappa-B Activity

LABORATORY: NIS Laboratory Inc., Klamath Falls, OR

In a preliminary study on the phosphorylated form of NFkB on primary human leukocytes measuring the increase in fluorescence intensity over untreated cells, EpiCor caused higher levels of phosphorylated NFkB than lipopolysacccharides (LPS), using a new fixation method. When gating on the very core of the polymorphonuclear (PMN) population, this was even more pronounced.





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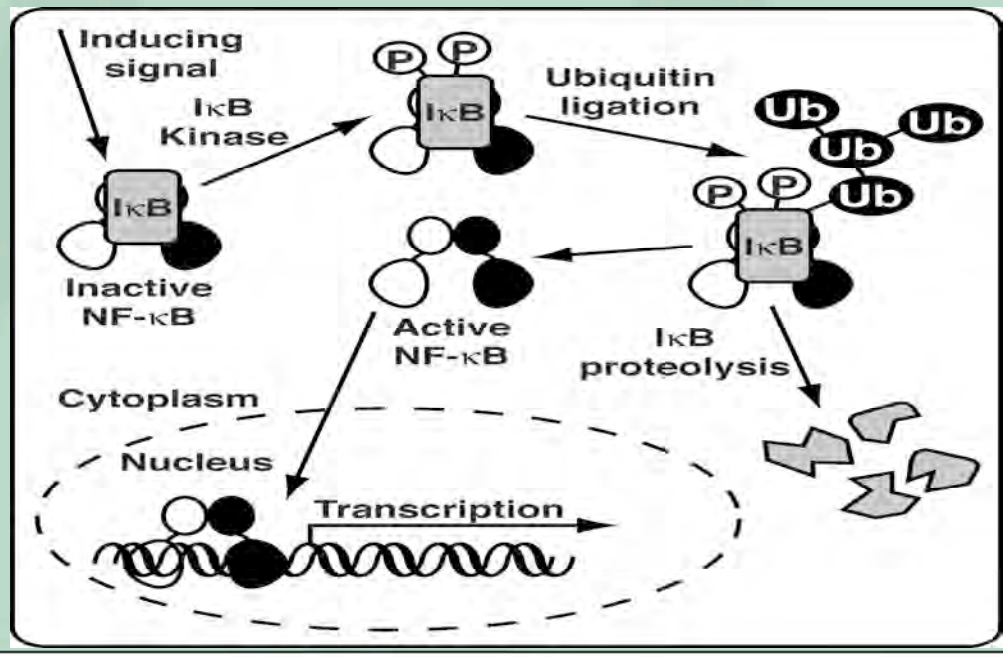
NF-kB plays an important role in inflammation, immunity, autoimmune response, cell adhesion, cell proliferation (growth), development, and cell death (apoptosis), by regulating the expression of genes involved in these processes.

NF-kB is present in most resting cells as an inactive complex with a member of the I-kappa-B family of transcription factor inhibitor proteins. In response to inducing stimuli, such as cytokines and growth factors, viral and bacterial products, physical or environmental stresses, and chemotherapeutic drugs, the complex-associated I-kB molecule becomes degraded. Removal of I-kB converts NF-kB to its active form.



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Modulation of Adhesion Molecules and Calcium Signaling in Human Lymphocytes *in vitro*

LABORATORY: NIS Laboratory Inc., Klamath Falls, OR

RESULTS:

I. EpiCor modulates the expression of:

- L-selectin (CD62L, an indicator of initial interaction of circulating cells with the endothelium) on human B cells and NK cells
- B2 integrins (CD11a, an indicator of homing and signaling) on both B cells and NK cells
- B1 integrins (both CD29, CD49d, indicators of migration on the extracellular matrix after tissue entry) on both B cells and dendritic cells

II. EpiCor induces calcium signaling.

CONCLUSION:

These results indicate that EpiCor appears to modulate the expression of certain adhesion molecules on human NK cells, T cells, B cells, and dendritic cells *in vitro*, as well as induce calcium signaling.

Importance of Calcium Signaling between Cells

Signaling is pivotal to the coordinated response of cells in tissues and organs within the whole body.

It is now well established that cells do not behave as selfish entities but rather tend to form “micro-societies” whose proper functioning requires a precise coordination of emission and reception of signals. Dysfunctioning of the networks is associated with pathological situations that can range from abnormal proliferation to death. This is why the finding that EpiCor facilitates calcium signaling between cells is important, for it may explain in part how it enhances immune response to potentially invasive or invasive pathogens.

An Open-Label, Single-Dose Phase I Study in Healthy Adults

LABORATORY: Radiant Research, Inc., Chicago, IL

OBJECTIVE: To assess the influence of oral ingestion of 500 mg per day of EpiCor on mucosal and cell-mediated immunity.

METHOD: (as described already in PART III: Toxicity/Safety Studies)

- Subjects (n=15, men and women aged 18-40) received 500 mg of EpiCor in a single daily dose for 30 days.
- Immune function parameters were measured in blood and saliva samples taken on Days 0, 14, 21, and 28 by *Immunosciences Lab*.

RESULTS:

- Mean group salivary IgA increased (but not significantly) by 72%, 51%, and 59% after 14, 21, and 28 days of supplementation, respectively.
- Median IL-2 decreased significantly by 68% ($p<0.01$) on day 21 of supplementation and showed high inter-subject variability.
- Mean NK cell cytotoxic activity increased by 3-3.5% at days 14 and 21, but decreased by 55% at day 28. These changes were not significant.
- Lymphocyte subpopulation analysis revealed a significant decrease in percent CD8 (suppressor cells, $p=0.03$) leading to a significant increase in CD4(helper)/CD8 ratio ($p=0.02$) at day 28.

An Open-Label, Single-Dose Phase I Study in Healthy Adults(continued)

CONCLUSIONS:

- The increase in salivary IgA indicates that treatment with EpiCor may be associated with the development of mucosal immunity.
- The significant decrease in the number of suppressor cells with EpiCor treatment resulted in a better ratio of helper to suppressor cells.
- (Note: immunologic or pharmacologic manipulation of regulatory T-cell populations represents an important approach to immunotherapy of a wide range of immune responses.)

GRAS Elements

GRAS Self-determination requires an expert panel to review the ingredient's:

- Background
- Composition and characterization
- Manufacturing/production methods
- Intended use(s)
- Estimated daily intake, and
- Safety/toxicological assessment

Self-Affirmed GRAS Status

EpiCor GRAS Expert Committee Members

Chair: Theodore M. Faber, PhD, DABT

- FDA 20 years (Previously, Director, Division of Drug and Environmental Toxicology, Human Food Safety Program; Acting Associate Director for Regulatory Evaluation, Division of Toxicology, Bureau of Foods, etc.)
- EPA 4 years (Previously, Chief, Toxicology Branch: Director, Health Effects Division)

Norbert Page, PhD, DABT

- EPA (Previously, Director of EPA Scientific Affairs for Toxic Substances and Pesticides; and Chief, NIOSH Priorities and Research Analysis Branch.Director of Scientific Affairs, Office of Toxic Substances, etc.)
- NIH (Previously, Director of the NCI's Carcinogen Testing Program; Chief, Office of Hazardous Substances Information, National Library of Medicine)
- Past President of the Society of Toxicology

Joseph Borzelleca, PhD, DABT

- Professor Emeritus, Pharmacology and Toxicology, Medical College of Virginia.
- Former, Chairman of the Board on Toxicology, Food Chemicals Codex Committee
- Consultant to FDA, NIH, NCI, NATO, FAO/WHO, US Army, ILSI, etc
- Editor, Food and Chemical Toxicology
- Past President of the Society of Toxicology

Result: Expert panel declares that EpiCor is Self-Affirmed as GRAS


EPICOR™