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Clinical Study Report

Protocol No: BNL-001

Interventional / Prospective, Phase I Study To Evaluate The Safety Of RECEPTOL® Oral Spray Used As A Stand-Alone Mono Therapy in HIV /AIDS Patients with multiple symptoms

1. TITLE PAGE

STUDY TITLE	Interventional / Prospective, Phase I Study To Evaluate The Safety Of RECEPTOL® Oral Spray on Patients Infected with HIV
PROTOCOL CODE	BNL-001
NAME OF INVESTIGATIONAL PRODUCT TESTED	RECEPTOL® Oral Spray
DEVELOPMENT PHASE OF STUDY	Phase I
INDICATION STUDIED	HIV/AIDS
TRIAL DESIGN	Interventional / Prospective, 30-days study in 12subjects to determine safety of RECEPTOL® on patients with HIV / AIDS.
STUDY INITIATION DATE	February, 1996
STUDY COMPLETION DATE	April, 1996
SPONSOR	Biomix Network Limited A2101 -04, Mansarovar, Neelkanth heights , Pokhran Rd 1 , Thane West 400606, India What's all contact : +91 82910 84108
PARTICIPATING INSTITUTE	**PRINCIPAL INVESTIGATOR: Dr. Steve Mathews** **INVESTIGATOR: Dr.Robert Brandt, MD** **STUDY CENTER:** Infectious Disease Clinic, Dayton, Ohio, USA

2. SYNOPSIS

NAME OF THE PRODUCT

- RECEPTOL® Oral Spray

ACTIVE INGREDIENTS

- RADHA 108 Series and Proline Rich Peptides (PRP)

TITLE OF THE STUDY

- Interventional / Prospective, Phase I Study To Evaluate The Safety OfRECEPTOL® Oral Spray on Patients Infected with HIV.

STUDY SITE

- Infectious Disease Clinic, Dayton, Ohio, USA

TREATMENT PERIOD

- 30 Days

OBJECTIVES

Primary Objective

To evaluate the Safety of RECEPTOL® liquid in HIV/AIDS patients in terms of reporting any Adverse event (AE) and Serious Adverse Event (SAE).

Secondary Objectives

To determine the effect of oral spray administration of RECEPTOL® liquid on:

- Change in Body weight gain of patients
- An improvement in the quality of life as observed by patients.
- Ascertainment of disease progression or clinical deterioration (development of HIV-related features, for instance, incidence of Chronic Diarrhoea, Nausea, Vomiting etc.).
- An improvement in the nutrition status as an indirect marker of improved quality of life, by monitoring various nutrition indices
- An improvement in the performance of patients immune system.

METHODOLOGY

- This trial was a 30 days study to evaluate the safety of RECEPTOL® liquid inHIV/ AIDS patients.
- The study was designed to investigate safety of RECEPTOL® therapy by reporting any Adverse event (AE) and Serious Adverse Event (SAE).
- The study subjects received RECEPTOL® liquid as a spray self-administered by patients on either side of the oral buccal surface 6 times daily at every 4 hour's interval. Each administration consisted of 3 sprays directly on the buccal mucosa.

NUMBER OF PATIENTS

- A total of 12 patients completed the study.

INCLUSION CRITERIA

For recruitment in the study, the subjects were required to be :-

- If available, patients' pre-diagnoses report HIV sero-positive.
- Patient who are symptomatic or asymptomatic.
- Patients who are ≥ 18 years of age.
- Patients who are willing to gain or maintain a proper diet and drink 5-8, 8 ounce glasses of water per day.

EXCLUSION CRITERIA

Patients were not included in the study if they were :-

- Patients treated with any other investigational drug(s) within the last 30 days before the study begins.
- Patients who are, think they might be or plan on becoming pregnant.

CRITERIA FOR EVALUATION

- The safety assessments consisted of monitoring and recording all Adverse Events including Serious Adverse Events.
- The efficacy variables were improvement in HIV associated clinical symptoms and physical findings and increase in body weight of patients.

STATISTICAL METHODS

- The clinical, physical and laboratory measures obtained from the patients "Symptom Assessment Form" were analyzed by appropriate descriptive and non- descriptive statistics.

STUDY RESULTS

Safety Results

- All patients tolerated RECEPTOL® well with No Adverse or Serious Adverse Events reported.

Efficacy Results

- **Body Weight Gain**: A significant increase was evident in bodyweights of all the most HIV positive patients who completed the trial treatment. 10 out of 12 patients gained weight and of these 10, 7 patients gained on an average 6 of lbs. The highest weight gain of 12 lbs was recorded for a patient who had been HIV positive since 10 years.
- **Improvement in Clinical Symptoms**: All 12 patients experienced an improvement in their overall symptom assessment score and average reduction approached 63%.

CONCLUSION

- The 30 days trial treatment with RECEPTOL® was well tolerated with no incidence of any side effects reported in any of the patients studied.
- HIV associated clinical and physical symptoms also improved with the therapy and most of the patients gained weight during the 30-day trial period.

3. STATEMENT OF COMPLIANCE

This study was conducted in compliance with the Protocol as well as the Sponsor's and CRC's (CRO) **Standard Operating Procedures**. These were designed to ensure adherence with the ethical principles that have their origin in the **Declaration of Helsinki, Good Clinical Practice (GCP)** and applicable regulatory requirements.

4. LIST OF ABBREVIATIONS AND DEFINITIONS

List of Abbreviations

- **AIDS** Acquired Immunodeficiency Syndrome
- **ART** Anti-Retroviral Therapy
- **ARS** AIDS Related Complex
- **CD4** Cluster Of Differentiation 4
- **CD8** Cluster Of Differentiation 8
- **CHF** Congestive Heart Failure
- **CRC** Clinical Research Coordinator
- **CRO** Contract Research Organization
- **CDSCO** Central Drugs Standard Control Organization
- **cmm** Cubic Millimeter
- **DCGI** Drug Controller General of India
- **DGHS** Director General Health Services
- **dL** Deciliter
- **ELISA** Enzyme Linked Immuno Sorbent Assay
- **GCP** Good Clinical Practice
- **HIV** Human Immunodeficiency Virus
- **ICMR** Indian Council Of Medical Research
- **IIH** Institute of Immuno-Heamatology
- **INF** Interferon
- **LFT** Liver Function Test
- **mm3** Per cubic millimetre
- **ml** Millilitre
- **mg** Milligram
- **NACO** National AIDS Control Organization
- **NKC** Natural Killer Cell
- **NNRTI** Non-Nucleoside Reverse Transcriptase Inhibitor
- **NRTI** Nucleoside Reverse Transcriptase Inhibitor
- **PCR** Polymerase Chain Reaction
- **PRP** Proline-Rich Polypeptide
- **TNF** Tumor Necrosis Factor
- **WBC** White Blood Corpuscle
- **WHO** World Health Organization

Definitions of Terms

- **Eligible:** Qualified for enrolment into the study based on strict adherence to inclusion and exclusion criteria.
- **Evaluable:** Meeting all eligibility criteria, complying with the procedures defined in the Protocol and therefore included in analysis.
- **Investigator:** Treating physician
- **Subject(s):** Term used throughout this report to denote the enrolled individual(s)

5. TABLE OF CONTENTS

6. ETHICS COMMITTEE

This study was conducted in accordance with the ethical principles of Declaration of Helsinki. Ethical approval of the Study Protocol was obtained from the Local Ethics Committee at Infectious Disease Clinic, where the study was conducted before the study was undertaken. The original documents were sent to Sponsor and the Investigator filed a copy. In addition, all local regulatory requirements will be adhered to. All attempts will be made to afford greater protection of study patients.

The Investigator/Institution has written and dated approval from the EC for the following: Study Protocol/Amendment(s), written Informed Consent Form including patient information sheet, consent form updates and patient recruitment procedures (e.g. advertisements).

7. INTRODUCTION

Introduction: HIV/AIDS and Types of Treatment:

The advent of HIV/ AIDS has graphically demonstrated that our knowledge of viruses and how to treat viral infections was not adequate. According to the joint United Nations program on HIV / AIDS and World Health Organization (WHO), some 25 million people have died of HIV / AIDS in the past 25 years and an estimated 38.6 million are infected with the virus, making it one of the most lethal epidemics in the history of mankind.

Currently five classes of drugs are approved by US FDA for treatment of HIV infected patients. These five classes are Nucleoside Reverse Transcriptase Inhibitor (NRTI/NtRTI), Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), Protease Inhibitor (PI), entry inhibitors and Integrase Inhibitor. Anti Retroviral Therapy (ART) regimen is complicated due to the high cost of treatment, poor compliance, pill burden, peculiar storage requirements, drug-drug interactions, co-morbidities like tuberculosis, liver disease, cardiovascular complications and importantly treatment failure due to resistance to drugs acquired by the virus through mutation. All the antiviral drugs developed so far to fight HIV infection, exhibit serious side effects like nausea, Diarrhoea, Vomiting, Pancreatitis, Anemia, Peripheral Neuropathy, Lactic Acidosis, Dyslipidemia and others. Currently, the US FDA has approved 29 drugs for use in the treatment of HIV Infection[5]. The presently available ART is very expensive. The future outlook for HIV / AIDS treatment from a pharmaceutical perspective remains bleak despite significant gains in understanding of the virus. This situation has forced scientists to look for alternative effective solutions.

A promising alternative which may prove more effective can be to stimulate the body's own defenses against the virus as well as the infected cells. Dietary supplementations of many naturally occurring substances have been claimed to boost human immunity by activating human Natural Killer (NK) cell activity.

One such area of investigation is based on an age-old remedy, the Colostrum, the first milk produced by a mammal following the birth of a newborn, which was widely used as an immunity booster and natural antibiotic before modern antibiotics were developed. Colostrum and various components of it have already been demonstrated to be useful in treating opportunistic infections associated with HIV/ AIDS such as Diarrhea etc. caused by Clostridium, Campylobacter and Amoeba spc.[13.] Specifically one of the components of Colostrums, the nano-

peptides classified under Radha 108 series (Patent pending by Biomix Network Ltd.) and the Proline Rich Polypeptide (PRP) – Infopeptides has shown great promise. This unique polypeptide (a peptide fraction of whole Colostrum) has been shown to exhibit Immunomodulatory activity as well as antiviral activity[14]. The advantage of these compounds over conventional antiretroviral drugs is that these display a much shorter response time for alleviation of physical and clinical symptoms of the disease and a relatively quick normalization of NK activity. It is the only Immunomodulator produced by mammals themselves for their progeny. The key factor is however, the protein fractionation and ultra filtration technology needed to extract RADHA 108 and Proline-Rich Polypeptide (PRP) extraction which is developed now by Biomix Network Ltd using patented technology and molecular weight exclusion columns to ensure consistency of product batch after batch in every bottle of RECEPTOL®.

Rationale for this study

There is an imminent need for additional lines of nutritional defense against the potential ravages of both infectious and non-infectious disease processes which currently plague people all around the world, from all walk of life, at all stages in the life cycle and which promise to incur irreversible harm to human health and well-being.

Nutrition Associated Immune Deficiency Syndrome (NAIDS) is, in fact, the greatest threat to our global population and the initiating syndrome for a myriad of other menacing and currently unmanageable disease states.

Many agents for the treatment of AIDS caused by Human Immunodeficiency Virus (HIV) are becoming available for testing, including vaccines, antiviral drugs, immunostimulating agents and other drugs. We have no reason to suspect, nor do we claim that RECEPTOL® is a cure or prevention of AIDS.

However, we have reason to expect that regular consumption of RECEPTOL® may prevent certain opportunistic infections, since inherent in RECEPTOL® are some of the infopeptides that instruct the host to defend itself. Therefore these infopeptides, in conjunction with the complete energy, protein, vitamin, mineral and other novel components present in the product, may alleviate or improve some of the symptoms associated with opportunistic and bacterial infections, such as with diseases like AIDS.

RECEPTOL®: Product Development Rationale

The application of RECEPTOL® is, in the medical field of Immuno-therapy which is a quiet revolution taking place in medicine. It is a form of treatment that uses the different aspects of your immune system, its cells and molecules and its various stratagems to tip the balance in your favor as your body battles to maintain health.

RECEPTOL® comes to us after nearly fifty years of research and over 3,500 scientific medical papers, which prove its effectiveness. It is found in colostrum and is a natural way of strengthening our immune systems against disease.

RECEPTOL® contains the Nano-Informational Peptides (RADHA108) and Proline-Rich Polypeptides (PRPs), derived from bovine Colostrum, which helps in strengthening the body's own immune system against diseases in a natural way.

The nano-polypeptides have been known for long for their antiviral, anti-inflammatory and immune enhancing properties. However, the molecular mechanism of their action in conjunction with low molecular weight nano-peptides was not known until *Dr. Theodore Damodar Singh*, an Applied Biochemist from University of California Irvine and Founder Director, Chaitanya Healthcare, India and Dr. Pawan Saharan, Chief Scientific Officer and Founder Director, Chaitanya Healthcare and Biomix Network Ltd., India identified and studied a series of *Nano-Informational Peptides (RADHA108$_{1-100}$)* from Bovine Colostrum.

The fusion of viral particles with human white blood cells occurs with the aid of glycoprotein epitopes on the viral wall. The informational proteins (RADHA108$_{1-100}$) in RECEPTOL® have been shown to mitigate cell fusion. The RADHA108$_{1-100}$ series of molecules may dock on the glycoprotein receptors of the viral surface mimicking their receptors on the cell surfaces and thus block the virus entry into the immune cells.

One of the Immunomodulatory action of RECEPTOL® is to stimulate the maturation of immature thymocytes into either helper or suppressor T cells[4,5], depending on the need of the body at a given time. Helper T cells present antigens (such as viral protein) to B lymphocytes, which in turn produce antibodies to that antigen[6]. Helper T cells also help produce memory T cells which retain the memory of an antigen in order to expedite the production of antibodies in the event the antigen is reencountered in the future[7].

Suppressor T cells, on the other hand, have been shown to deactivate other lymphocytes after an infection has been cleared to avoid damage to healthy tissues[8]. RECEPTOL® may also promote growth and differentiation of B cells in response to an infection[9] and the differentiation and maturation of macrophages and monocytes[10.] The activity of Natural Killer (NK) cells, cytotoxic cells of the innate immune system, is increased by up to 5-fold by RECEPTOL®[11, 12].

RECEPTOL® may modulate the cytokine system as well. Its constituents have been shown to stimulates the production of a wide range of cytokines, including the pro-inflammatory cytokines Tumor Necrosis Factor – Alpha (TNF-α) and Interferon Gamma (INF–γ) and anti-inflammatory cytokines Interleukin – 6 and – 10[13].

The constituents of RECEPTOL® may function as a molecular signaling device which works through receptors on target cell surfaces[14] to initiate or suppress the production of specific proteins. This property is not species specific[2]; and hence the constituents of RECEPTOL® derived from bovine Colostrum may work as effectively in humans too like the PRP of human Colostrum. There are no known side effects or drug interactions with the constituents of Colostrum, and it may be taken safely by patients of all ages. In an experimental in vitro system, the constituents of RECEPTOL® have been shown to effectively block HIV infection of cells[15.] RECEPTOL® in combination with Zidovudine®, a known anti-retroviral drug, has been shown to be effective in patients suffering from HIV/AIDS Related Complex (ARC), effecting an increase in White Blood Cells, CD8 lymphocytes and IL-2[16].

RECEPTOL® has shown to be effective in treating many different diseases and conditions including Allergies, Thrush, Diabetes (type II), Rheumatoid Arthritis, Corneal Regeneration, Diarrhoea, Hemolytic Anemia, Tuberculosis, HIV, Hepatitis A & C, Acute Viral Infections, Pharangitis (Viral), Viral Respiratory Infection, Plantar Warts, Colds and Flues, Herpes Simplex I & II etc.

Safety

RECEPTOL® is a normal food substance and as such is as safe for human consumption as any other food. The safety of RECEPTOL® has been further verified over the years by distributing it in the United States as a food product.

Since RECEPTOL® is a food and not a drug, metabolism and excretion are non-issues. There are no known drug interactions. The only contraindication identified so far is intolerance to milk or milk products.

8 STUDY OBJECTIVES

Primary Objective

To evaluate the Safety of RECEPTOL® liquid in HIV/AIDS patients in terms of reporting any Adverse event (AE) and Serious Adverse Event (SAE).

Secondary Objectives

To determine the effect of oral administration of RECEPTOL® liquid spray on:

- Change in Body weight gain of the patients
- An improvement in the quality of life as observed by the patients.
- Ascertainment of disease progression or clinical deterioration (development of HIV-related features, for instance, incidence of Chronic Diarrhoea, Nausea, Vomiting etc.).
- An improvement in the nutrition status as an indirect marker of improved quality of life, by monitoring various nutrition indices.
- An improvement in the performance of the patients' immune system.

9 INVESTIGATIONAL PLAN

Overall Study Design and Plan: Description

- This study was trial, comprised of a 30 days treatment period. Patients obtained RECEPTOL® supplies (to last the entire study).
- At the initial study visit, Informed Consent was signed by the patients and obtained. The patient's inclusion and exclusion criteria was reviewed. A brief physical examination was performed, to asses the severity of the disease and the patient's weight.
- A follow up assessment of any adverse experience were recorded through out 30 days once a week. At the follow up visit, the physician filled out a "Symptom Assessment Form" for each patient. .
- Information regarding the patient's survivability progression, weight, and performance status was obtained and recorded on the Symptom Assessment Form provided.

Subject Selection Criteria

- The selection of subjects for this trial was based on the following Inclusion and Exclusion criteria.

INCLUSION CRITERIA

- If available, patients' pre-diagnoses report HIV sero-positive.
- Patient who are symptomatic or asymptomatic.
- Patients who are ≥ 18 years of age.
- Patients who are willing to gain or maintain a proper diet and drink 5-8, 8 ounce glasses of water per day.

EXCLUSION CRITERIA

- Patients treated with any other investigational drugs with 30 days before the study deigns.
- Patients who are, think they might be or plan on becoming pregnant.

Treatment Procedures

- RECEPTOL® liquid spray used in the study was a Colostrum product, containing natural microscopic molecules of $Radha_{108}$ of 800 – 1200 DaI molecular weight (below 2000 DaL that enable to cross bbb- Blood brain barrier) and PRPs consisting of oligoribonucleotides attached to a peptide molecule. RECEPTOL® was manufactured by Biomix Network Ltd., Mumbai by protein fractionation and ultra nano filtration technology the only nanotechnology based plant in India. Eligible patients were evaluated for medical history, physical examination, blood and urine tests, and other tests as determined by the Principal Investigator. Patients had received RECEPTOL® liquid in pump spray form and were taught to self-administer the medication. The frequency of dose administration was 3 sprays at every 4 hour intervals directly on the buccal mucosa (inner cheek). The patients were advised to gargle the medication in the mouth for 30 seconds before swallowing it. The trial treatment as described above was continued for a period of 30 Days.

Assessment Schedule

- At times 0 and 30 days, blood samples, on select patients, when feasible and at the discretion of the physician, will be withdrawn to ascertain the following information:
- White Blood Cell count
- Red Blood Cell Count
- Hemoglobin
- Hematocrit
- Erythrocyte Sedimentation Rate
- Chest X-ray (if applicable)

Compliance

- The test product, RECEPTOL® is provided as a liquid, which is be taken orally, three sprays every four hours around the clock.

Assessment of Safety Criteria

- Safety parameters were assessed by measuring the no. of Adverse and Serious Adverse Events.
- Clinical symptoms and Physical Findings which included HIV associated Fatigue, Diarrhoea, Nausea & Cough were assessed using Symptom Assessment Form which was recorded in patients every visit.

Statistical Methods Used

- The clinical, physical and laboratory measures obtained from the patients "Symptom Assessment Form" was analyzed by appropriate descriptive and non- descriptive statistics.

10 TRIAL SUBJECTS

A total of 12 patients were enrolled and all completed study without any drop-out. Thus, at the end of study, pre and post treatment data of 12 patients mentioning no. of Adverse and Serious Adverse Events and clinical symptoms was available for statistical analysis.

(Total no. of Patients Enrolled and Analyzed = 12)

11 STUDY RESULTS

Safety Evaluation

***Table Showing Primary Safety Parameters (AE and SAE) Measured At Baseline and At the End of 30 Days Treatment with* RECEPTOL®**

Patients	Baseline	Day 30
1	0	0
2	0	0
3	0	0
4	0	0
5	0	0
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	0	0

Safety/Tolerability assessments consisted of monitoring and recording all Adverse Events and Serious Adverse Events. All patients tolerated RECEPTOL® well with no side effects. Milk allergies are caused by the large milk proteins, primarily casein, and to a lesser extent the Immunoglobulins. These proteins are completely removed from the RECEPTOL®. As RECEPTOL® is a food substance derived from Colostrum, it was found to be safe for human consumption.

Table Showing Clinical Symptoms at Baseline and At the End of 30 Days Treatment with RECEPTOL®

Symptom	Initial/total No. of pt	Reduction No. of pt	Elimination No. of pt
Diarrhoea	8/12	6	5
Fatigue	9/12	9	9
Nausea	8/12	7	5
Cough	4/12	3	2

8 out of 10 patients had various levels of diarrhoea (mild, moderate or severe) at the beginning of the trial period. Out of the 8, 5 patients (62%) went from varying levels of diarrhoea severity to No diarrhoea symptoms. The 1 patient without weight gain experienced total elimination of severe chronic diarrhoea and a return to solid stool formation. 8 out of 12 patients had various levels of nausea at the beginning of the trial period. Of the 8, 5 patients (62%) went from varying levels of severity of nausea symptoms to No nausea. Of the remaining 3 patients, with some degree of nausea, 2 experienced a reduction in the severity of their symptoms. 9 out of 10 patients, who reported fatigue symptoms at the beginning of the trial, experienced an increase in their level of energy. 4 out of 12 had either a mild to moderate cough at the beginning of the trial. 2 of the 4 reported No cough at the end of the trial period. Of the remaining 2 patients, 1 reported a reduction in the severity of his cough.

12 DISCUSSION AND OVERALL CONCLUSIONS

- The trial was conducted in 12 HIV patients with 30 days treatment and moderate control of product use. Results obtained from this trial were 10 out of 12 patients gained weight during the thirty-day trial period, of the 10 that gained weight, 7 (70%) gained an average of 6 lbs, 5 patients gained 6 lbs in one month, while 2 others gained 5.5 and 6.6 lbs respectively, the highest weight gain of 12 lbs was recorded for a patient who had been HIV positive since 1986 (10 years). 8 out of 10 patients had various levels of diarrhoea (mild, moderate or severe) at the beginning of the trial period. Out of the 8, 5 patients (62%) went from varying levels of diarrhoea severity to No diarrhoea symptoms. The 1 patient without weight gain experienced total elimination of severe chronic diarrhoea and a return to solid stool formation. 8 out of 12 patients had various levels of nausea at the beginning of the trial period. Of the 8, 5 patients (62%) went from varying levels of severity of nausea symptoms to No nausea. Of the remaining 3 patients, with some degree of nausea, 2 experienced a reduction in the severity of their symptoms. 9 out of 10 patients, who reported fatigue symptoms at the beginning of the trial, experienced an increase in their level of energy. 4 out of 12 had either a mild to moderate cough at the beginning of the trial. 2 of the 4 reported No cough at the end of the trial period. Of the remaining 2 patients, 1 reported a reduction in the severity of his cough. All 12 patients experienced an improvement in their overall symptoms assessment score. The average reduction approached 2/3 (63%).

13 LIST OF REFERENCES

1. Khan A. Non-specificity of transfer factor. Annals of Allergy 38(5):320-322 (1977)

2. Immunology, Immunopathology and Immunity. Sell S. Appleton and Lange: Stamford CT 1996.

3. Janusz M, Staroscik K,Zimecki M,Wieczorek Z,Lisowski J. A proline-rich polypeptide (PRP) with immunoregulatory properties isolated from ovine Colostrum. Archivum immulologiae et therapiae experimentalis (Warszava) 34(4):427-436 (1986)

4. Wieczorek Z, Zimecki M, Spiegel K ,Lisowski J, Janusz M. Differentiation of T-cells into helper cells from immature precursors : identification of a target cell for a proline-rich polypeptide(PRP) Archivum immulologiae et therapiae experimentalis (Warszava) 37(3-4):313-322 (1989)

5. Bishop GA, Haxhinasto SA, Slunz LL, Hostager BS. Antigen-specific B-lymphocyte activation. Critical reviews in Immunology 23(3):159-197(2003).

6. Shi M,Hao S,Chan T,Xiang J. CD4+ T cells stimulate memory CD8+ T cell expansion via acquired pMHC I complexes and costimulatory molecules, and IL-2 secretion. Journal of leucocyte Biology (2006).

7. Zimecki M,Staroscik K, Janusz M, Lisowski J, Wieczorek Z. The inhibitory activity of proline-rich polypeptide on the immune response to polyvinyl pyrrolidone (PVP). Archivum immulologiae et therapiae experimentalis (Warszava) 31(6):895-903 (1983)

8. Julius MH, Janusz M, Lisowski J. A colostral protein that induces the growth and differentiation of resting B lymphocytes. Journal of Immunology 140(5):1366-371 (1988)

9. Kubis A, Marcinkowska E, Janusz M,Lisowski J. Studies on mechanism of action of a proline-rich polypeptide complex (PRP) : effect on the stage of cell differnciation. Peptides 26(11):2188-2192(2005)

10. Effects of oral dietary supplimentation with Ai/E$^{10®}$ upon Natural Killer (NK) cell activity in a healthy human population. Quantum Research, Inc., Scottsdate, Arizona(2001)

.

11. An examination of Immune Response Modulation in Humans by Ai/E[10®] Utilizing a double blind study. Immune Consultants, Inc., Tucson, Arizona (2001).

12. Zibiocka A, Janusz M, Rybka K, Wirkus-Romanowska I, Kupryszewski G, Lisowski J. Cytokine inducing activity of a proline-rich polypeptide complex (PRP) from ovine colostum and its active nonapeptide fragment analogs. European Cytokine Network 12(3):462-467(2001)

13. Modulation of 4HNE-mediated signaling by a proline-rich polypeptides from ovine Colostrum. Journal of Molecular Neuroscience 20(2):125-134 (2003).

.

14. Fernadez-ortega C, Dubed M, Ruibal O, Vilarruba OL, Menendez de San Pedro JC, Navea L, Ojeda M, Arana MJ. Inhibition of in vitro HIV infection by dialysable leucocyte extracts. Biotherapy 9(1-3):33-40 (1996)

.

15. Raise E, Guerra L, Viza D, Pizza G, De Vinci C, Schiattone ML, Rocaccio L, Cicognani M, Gritti F. Preliminary results in HIV I infected patients with transfer factor (TF) and zidovudine (ZDV). Biotherapy 9(1-3):49-54 (1996)

16. Claes-Henrik Floren S, Chinenye L, Elfstrand C, Hagman I, Ihse. Coloplus, a new product based on bovine Colostrum, alleviates HIV-assoiated diarrhoea .Scandinavian journal of Gastroenterology 2006; 41:682-686.