

THE DEVELOPMENT OF NICOSAN™/HEMOXIN™
A DRUG FOR THE MANAGEMENT OF SICKLE CELL DISEASE.

7.0 HISTORICAL BACKGROUND

NICOSAN™/HEMOXIN™ (formerly NIPRISAN) is a drug first developed by the National Institute for Pharmaceutical Research and Development (NIPRD) for the management of Sickle Cell Disease (SCD). It consists of a mixture of extracts from four tropical plants some of which are cultivated and others found in the wild both within and outside Nigeria.

The story of NICOSAN™/HEMOXIN™ will be incomplete without acknowledging some of the great minds, which have contributed immensely towards its development. Historically, a similar remedy was mentioned in the book titled “Iwosan” published by the late Dr. Odumosu at the turn of the century. However, the modern day origin of what later became patented as NIPRISAN was due to the late Rev. Paul Ogunyale, then Pastor of the First Baptist Church in Ibadan, Oyo State, Nigeria, who brought the attention of Prof. Charles Wambebe, former Director General, NIPRD in late 1992 to a herbal recipe of the drug.

From 1992 to 2001, Prof. Wambebe and his team of researchers at NIPRD, supported by the Federal Government of Nigeria (FGN) and the World Health Organization (WHO), worked tirelessly to develop NIPRISAN as a potent drug for the management of SCD and was patented in the United States of America under the leadership of Prof. Wambebe. After the retirement of Prof. Wambebe from NIPRID, his successor, Dr. Uford S. Inyang continued tirelessly with more developmental work in taking NIPRISAN to a higher level.

7.1 THE BIRTH OF NICOSAN™/HEMOXIN™

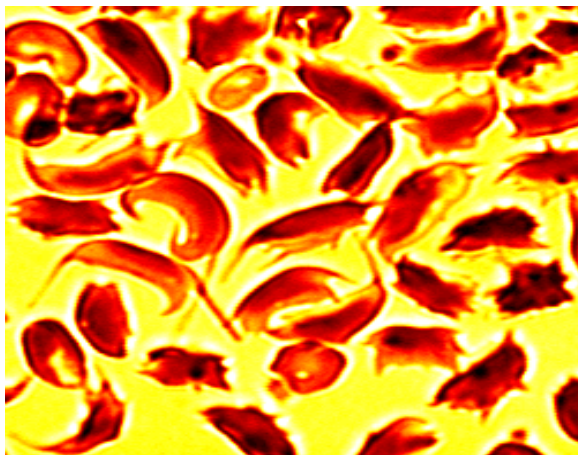
In August 2001, a joint conference on biotechnology was organized at Cook College, New Brunswick, NJ between the Sheda Science and Technology Complex (SHESTCO), Abuja and Rutgers University under the leadership of Dr. Soji Adelaja, who was then Dean of Research at Cook College and New Jersey Agricultural Experiment Station (Cook/NJAES), and Dr. Albert Ayeni, then Weed Scientist at Cook/NJAES and currently Coordinator of International Programs of Cook/NJAES.

Dr. Ramesh C. Pandey, Chairman & CEO, Xechem International, Inc., represented his company at this conference. What transpired during and after the conference propelled Dr. Pandey to explore the possibilities in the applications of biotechnology for drug production in Nigeria. At the instance of Prof. Turner T. Isoun, the Honourable Minister of Science and Technology, Dr. Pandey visited Nigeria for the first time in October 2001 with Dr. Albert Ayeni. This visit aroused in Dr. Pandey the interest in exploiting biotechnology for drug development in Nigeria. The first product of interest, NIPRISAN was thus, introduced to him by Dr. Ayodele Coker, the Director-General of SHESTCO, and later by Dr. Uford S. Inyang, the Director-General of NIPRID.

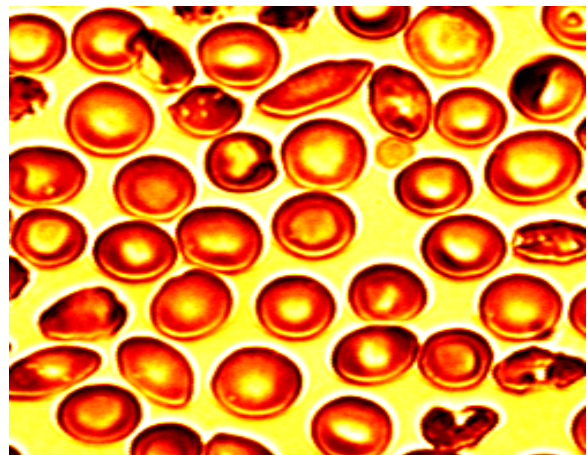
In July 2002, negotiations were successfully concluded between NIPRD and Xechem International under the direction of Prof. A. B. C. Nwosu, then the Honourable Minister of Health. Xechem International was granted the exclusive rights for development, production and marketing of NIPRISAN. To give effect to the agreement, Xechem Pharmaceuticals Nigeria Ltd, which is located within the premises of the Sheda Science and Technology Complex, was incorporated in 2002.

7.2 ABOUT SICKLE CELL DISEASE:

Sickle cell Disease is a genetic blood disorder caused by an abnormality in the hemoglobin molecule as depicted in the figure below. The condition causes the production of abnormal hemoglobin that contains portions that stick together after the release of oxygen. This phenomenon produces stiff, sickle shaped red blood cells that do not flow freely through blood vessels. These sickle shaped cells create clogs in the blood vessels, which prevent the flow of normal hemoglobin and oxygen round the body. The result is severe pain or “crises”, ulcers, organ and tissue damage and breakdown, which eventually lead to stroke and acute chest pain. The body’s immune system also attacks and seeks to destroy the abnormally shaped cells, often leaving the body with an insufficient number of normal oxygen-carrying red blood cells, which in turn results in anemic condition that manifest in fatigue and enhanced susceptibility to infection. It is estimated that there are 10 million sufferers of SCD worldwide, of which about 4 million are Nigerians.



Sickle Cells



Normal Cells

Repeated crisis can also result in damage to the kidneys, lungs, bones, eyes and the central nervous system. The most feared complication for children with SCD is a stroke which affects infants as young as 18 months. Many children with SCD do not survive infancy or early childhood. Adults with SCD often experience a reduction in the quality of life due to severe physical problems such as pain, Hard-foot syndrome and acute lung complications that can result in death. Frequent episode of severe bone pain, crises and hospitalization significantly affect the lives of these patients. It limits their ability to participate in normal physical activities, thus retarding their social

and economic advancement. It also deprives them of the joy of living life to the fullest and instills the fear of early death in them.

Before the advent for NICOSAN™/HEMOXIN™ the only known cure for the disease is a bone marrow transplant to replace defective red blood cells with donor healthy cells. Treatment has generally consisted of supporting therapies, which include folic acid for anemia, penicillin to prevent infections, pneumococcal and influenza vaccination, pain killing drugs and intravenous injection of fluids. In the United States of America, Hydroxyurea is the only drug approved by the Food and Drug Administration (FDA) for the treatment of SCD. It is very expensive and toxic and patients treated with hydroxyurea exhibit severe side effects.

7.3 HOPE FOR THE SICKLERS.

NICOSAN™/HEMOXIN™ is a non-toxic, phytopharmaceutical product composed of extracts from four tropical plants, seeds, stems, fruits and leaves. Each plant is indispensable in the manufacturing of NICOSAN™/HEMOXIN™. Xechem Pharmaceuticals Nigeria Limited has developed refined and standardized small-scale formulations of NICOSAN™/HEMOXIN™ for consistent production in strict compliance with the recommended procedures and policies of the WHO.

NICOSAN™/HEMOXIN™ has already undergone phase I and phase II clinical trials conducted in Nigeria by the NIPRD. Results from the phase III trials, if found satisfactory, will form the final basis for an application to the National Agency for Food and Drug Administration and Control (NAFDAC) for regulatory approval. Further laboratory testing among others have also been done at the National Heart, Lung and Blood Institute - Sickle Cell Disease Reference Laboratory (NHLBI-SCDR Lab) located at the Children's Hospital, Philadelphia, Pennsylvania, USA. The results of these trials show that NICOSAN™/HEMOXIN™ drastically reduced the degree of sickle cell formation, and the frequency and severity of SCD crises. Liver and kidney functions remained normal and patients gained appreciable weight. No adverse effects were reported during the trials. These clinical studies suggest that NICOSAN™ is a safe and efficacious phytomedicine for the management of SCD. It may have just paved the way for ending the misery and pain of millions of SCD sufferers in Nigeria and the world at large.

Through the instrumentality of Dr. Pandey, and based on the background of work done at the Children's Hospital, Philadelphia (CHOP) and other published literature in various indexed journals, on August 15th, 2003, NICOSAN™ (NIPRISAN) was granted an **Orphan Drug** status by the Food and Drug Administration of the United States of America (US-FDA). The Orphan Drug designation, entitles a company to various incentives including the waiver of Regulatory filing fees, access to potential funding for non-clinical and clinical research to generate required data for marketing approval, and seven years of marketing exclusivity once approved by the FDA.

This was a major break-through since it was a far-fetched possibility that the US-FDA would designate NICOSAN™ (NIPRISAN) Orphan Drug status. The Orphan Drug status has thus, added credibility and international acceptability to NICOSAN™ (NIPRISAN) as a potent drug for the management of SCD.