PROFILE OF SUCANON™

Background

Sucanon™ is the first member of a new class of diabetic drugs. Sucanon™ was discovered in the research laboratories of Biotech Holdings Ltd., in Vancouver, British Columbia. The discovery of Sucanon™ was an unexpected finding; scientists were working on Human Chorionic Gonadotrophin at the time, and not involved in diabetes research. An opportunity arose which allowed pre-clinical and clinical work to be done in China. Following the submission of an NDA in China, the drug was approved. The information contained in this document was drawn from the Chinese NDA and a selection was made to highlight pertinent elements to provide an overview of the current profile of Sucanon™. Supplementary clinical work in Mexico, carried out in 2012, has shown that the same sort of clinical activity can be reproduced in a non Asian population and has broadened the knowledge of this compound for prediabetic patients. Since 2010 PharmaRoth Labs Inc. under previous company name (Fero Industries Inc.) holds the intellectual property and other exclusive world-wide rights related to the production, marketing and distribution of Sucanon™, treatment for Type II Diabetes.

Compound

Sucanon™ is a small (421 daltons), water soluble, stable compound, that is simple to synthesize (four-step process) and formulate into tablets. If one compares it to other commercialized hypoglycemic agents on a mg per patient daily dosing basis, then Sucanon™ would appear to be a very potent member of its class, possibly several times more potent than insulin, and many hundred fold more potent than most commercialized hypoglycemic agents (daily dosing of up to 2 grams). The adult dose of Sucanon™ is around 2 mg per day.

Clinical Experience

The clinical benefits of Sucanon™ were convincingly demonstrated in a double-blind, randomized, placebo- & Glibenclamide controlled, multi-center, efficacy and safety study in 370 adult patients with Type II diabetes. DIAB IIT" was administered as tablets, one in the morning and one in the evening. The duration of the study was 6 months; four months treatment, preceded by one month screening evaluation, and followed by one month post-treatment follow-up. Glibenclamide is a commonly prescribed sulfonylurea, its benefits and limitations have been well known to diabetologists for over a decade. The parameters of response to therapy included an evaluation of the changes in clinical signs and symptoms of diabetes, an alteration in the blood and urine measurements of glucose metabolism, and an alteration in blood lipid levels.

The results indicated that the parameters of disease activity in patients receiving either Glibenclamide or Sucanon™ responded in a highly relevant clinical manner and that the differences from baseline measurements were statistically highly significant (p values <0.01). The lack of response in the group of patients who were randomized to receive placebo was also unequivocal, where the effect of administration was clinically small or non-existent, and the baseline to treatment difference was statistically insignificant (p value >0.05). An extract of the data is summarized in the following graphs and tables.

Table 1 Changes in glucose abnormalities in 370 Type II diabetic patients in 3 treatment groups of the randomized, double-blind, controlled study (before treatment and at the end of treatment analyses)

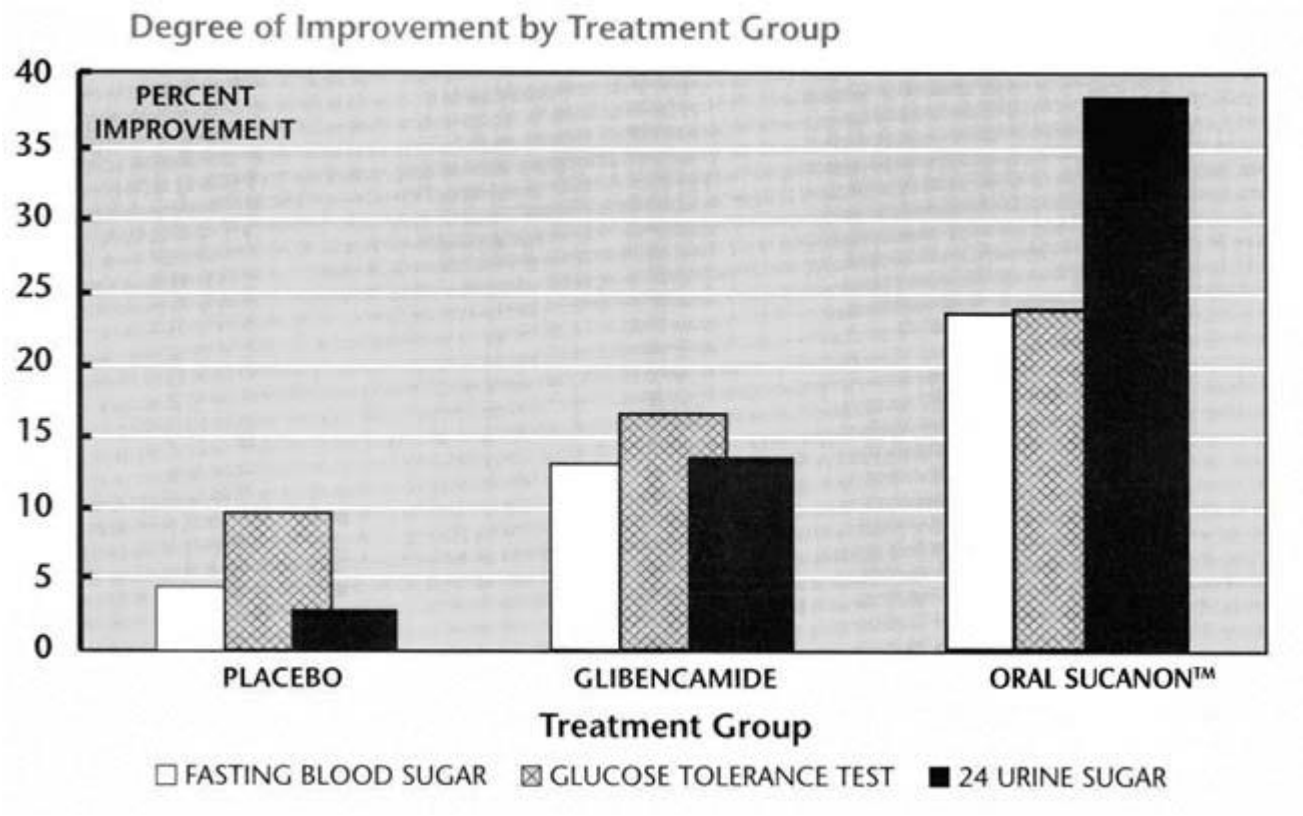
PARAMETERS					
	PLACEBO	Before	After	"t"	p
FASTING BLOOD SUGAR	(mmmol/L)	11.67 +/- 2.35	11.10 +/- 2.35	0.62	>.05
2-hr GLUCOSE TOLERANCE TEST	(mmmol/L)	17.67 +/- 6.01	15.99 +/- 5.27	2.29	>.05
24 URINE SUGAR	(g/24hr)	26.66 +/- 10.6	25.87 +/-12.5	0.96	>.05
	GLIBENCAMIDE	Before	After	"t"	p
FASTING BLOOD SUGAR	(mmmol/L)	11.27 +/- 2.18	9.79 +/- 1.65	4.54	>0.01
2-hr GLUCOSE TOLERANCE TEST	(mmmol/L)	17.13 +/- 3.20	14.27 +/- 2.22	6.18	>0.01
24 URINE SUGAR	(g/24hr)	27.3 +/- 6.85	23.59 +/- 6.09	6.7	>0.01
	ORAL SUCANON™	Before	After	"t"	p
FASTING BLOOD SUGAR	(mmmol/L)	12.55 +/- 3.13	9.60 +/- 2.38	9.23	>0.01
2-hr GLUCOSE TOLERANCE TEST	(mmmol/L)	17.99 +/- 5.20	13.68 +/- 4.42	8.74	>0.01
24 URINE SUGAR	(g/24hr)	21.55 +/- 11.5	13.30 +/- 8.95	0.78	>0.01

Table 2 Results from table 1 expressed as "Percent Improvement" (baseline to end of treatment)

PARAMETERS	PLACEBO	GLIBENCLAMIDE	ORAL SUCANON™
FASTING BLOOD SUGAR	4.50%	13.10%	23.50%
GLUCOSE TOLERANCE TEST	9.50%	16.70%	24.00%
DAILY URINE SUGAR	3.00%	13.60%	38.30%

Response to therapy was documented not only by a loss of, or a reduction in, disease related symptoms which included polyuria, polvdipsia, polyphagia, and fatigue, but also by the improvement in objective parameters of disease, namely, a reduction to normal or near normal levels in the elevated fasting blood glucose, and urinary sugar, and a normalization of the 100 g - oral glucose tolerance test. The objective results are given in table 1 above where the mean and standard deviations for these Values are listed, as well as the calculated "t" and "p" values. Given that the coefficient of variance of baseline values for the three treatment groups is small, and the patient number per group relatively large (n = 123), a between treatment group comparison is not unreasonable. These calculations (not shown) reveal that the improvements associated with therapy for both the Glibenclamide group of patients and the Sucanon™ group of patients were hoth better than placebo for all objective parameters measured, to a level that was statistically significant (p Values <0.05 to <0.01 respectively. This was not surprising from the t values listed in table 1. The difference in reduction of fasting blood glucose between the latter treatment groups was not statistically significant (p value >.0.05).

Figure 1 Improvement in glucose metabolism shown graphically

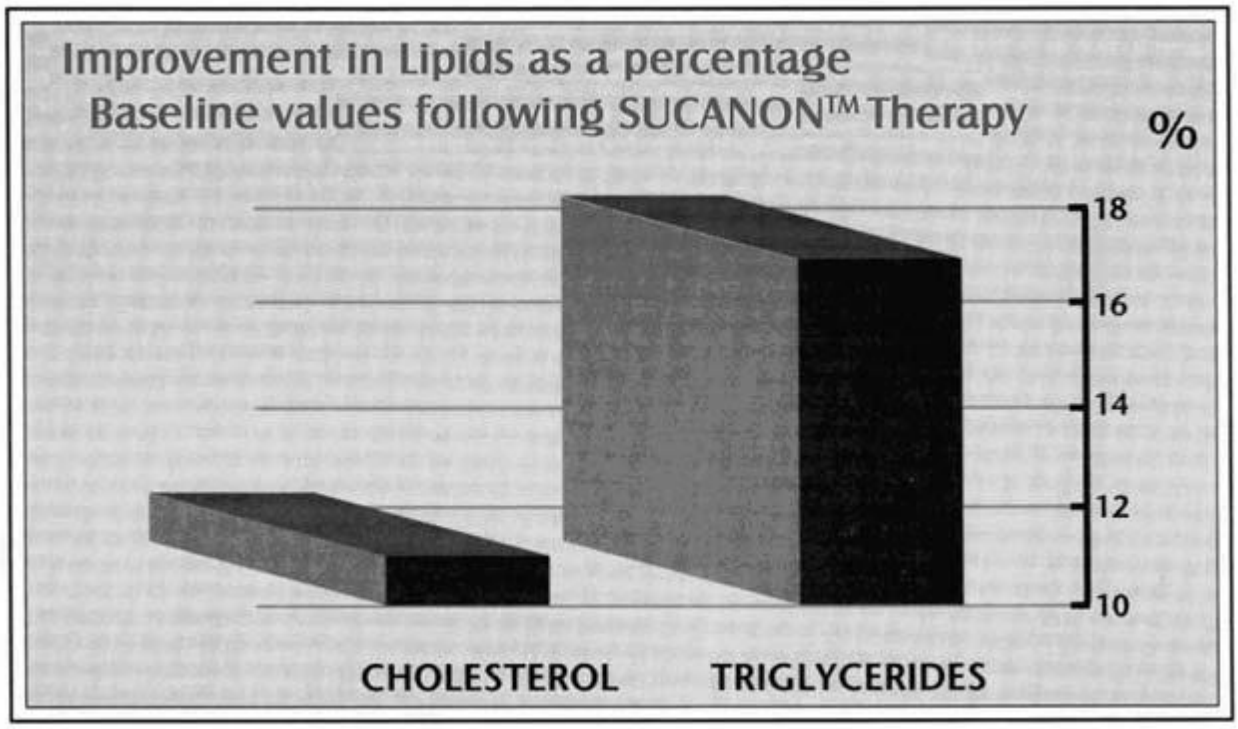


Elevated cholesterol and trigylceride levels in the blood were reduced to normal or near normal levels on Sucanon™ therapy. The level of reduction in cholesterol and triglyceride was clinically and statistically significant. These results are displayed in table 3 and figure 2 below.

Table 3 Sucanon™ associated improvements in blood lipid levels

FASTING LIPID		Before	After	"t"	p	% Diff
CHOLESTEROL	(mmol/L)	7.11 +/- 1.33	6.34 + 1.00	3.46	<0.01	11
TRIGYLCERIDES	(mmol/L)	2.34 +/- 1.07	1.94 + 4.73	4.73	<0.01	17

Figure 2 Improvements in blood lipids in diabetic patients on oral Sucanon™ therapy



A response analysis was done by the study coordinator in China and it was stated to be highly significant for Sucanon™ therapy with an overall response rate of 87%.

The toxicity profile (daily treatment for four months) was said to be difficult to distinguish from placebo.

Pre-clinical pharmacology

Pre-clinical in vivo and in vitro studies have identified that intravenous and oral Sucanon™ is pharmacodynamically active in diabetic rats, and out-performed all biguanides and sulfonylureas tested in those models. When added to rat muscle cells, its critical influence commences in seconds as it up-regulates insulin receptors, in a manner not yet understood, With the resultant increase in insulin endocytosis, uptake of glucose and L-leucine effects which last more than an hour.
In single-dose rat studies, peak response in lowering blood glucose takes 2 to 4 hours to occur, and the effect is lost by about 10 hours. Multiple oral dosing in rats (48 davs) and up to 4 months in man, shows no loss of activitv. Clear-cut pharmacological dose-response features were documented. Sucanon™ is also superior to other hypoglycemic agents in these models.

Figure 3 Effect of Sucanon™ on insulin receptor kinetics in rat muscle cells.

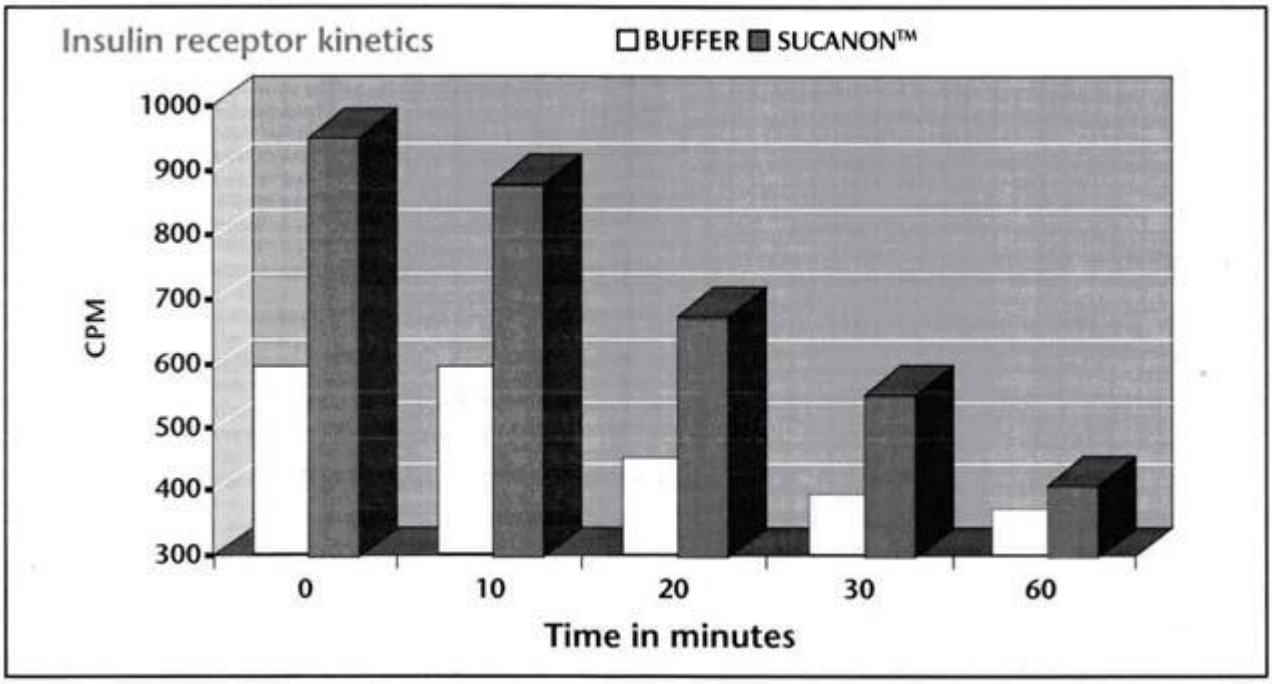
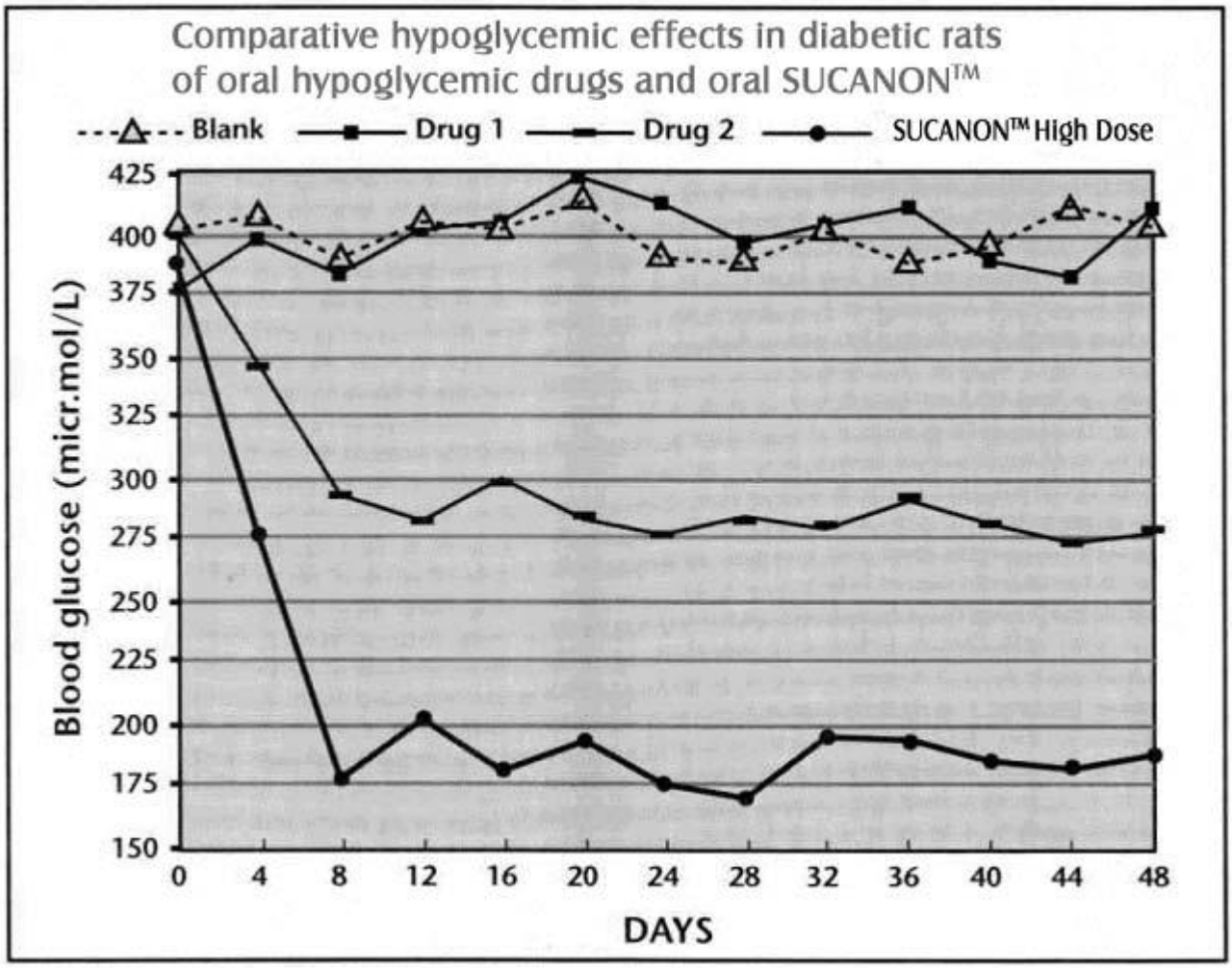


Figure 4 Oral Sucanon™ is superior to other biguanides and sulfonylureas in the rat diabetic model



Toxicity

The therapeutic index is so large (10,000 in mice) that its margin of safety must be unique in the armamentarium of drugs for the treatment of diabetes. Carcinogenicity, mutagenicity, and teratogenicity toxicities were not found in mice. Chronic dosing in dogs and rats at 2000 times the therapeutic dose was free of any toxicity.

Medical and Market Profile

Sucanon™ is a very potent member of a new class of drugs which can be described as fitting the profile of an insulin sensitizer. It could play a major role in the management of Type II diabetes alone or in combination with other drugs. It may even be helpful in Type I diabetes to reduce thE dose or prolong the benefit of injected insulin. DIAB II™ is a very active insulin sensitizer. Thf residual patent life for this drug when it is launched in the major markets will exceed any dru~ recently developed.