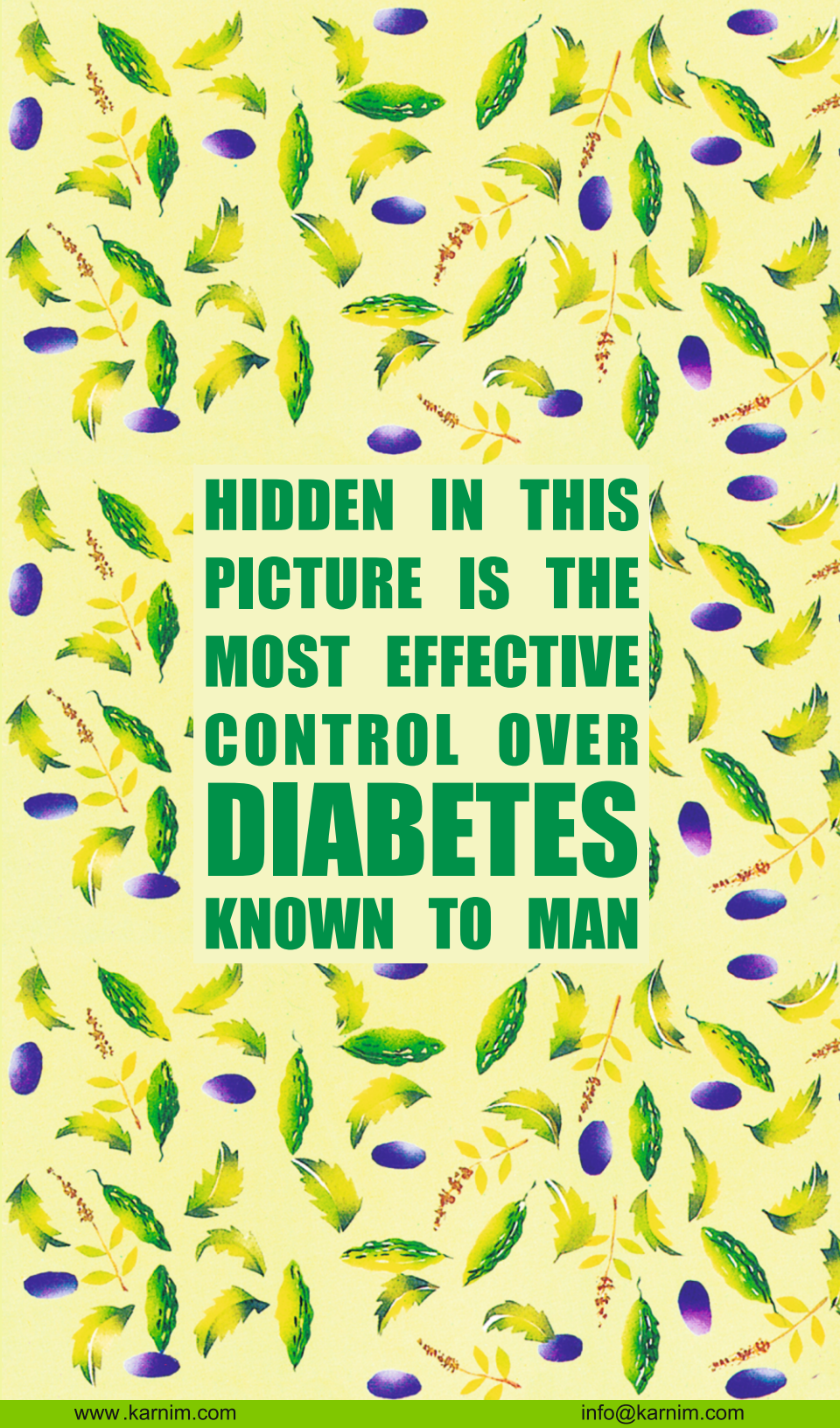

HIDDEN IN THIS PICTURE IS THE MOST EFFECTIVE CONTROL OVER DIABETES KNOWN TO MAN

KARNIM®

PRESCRIBING INFORMATION

KARNIM is indicated for patients with maturity onset diabetes mellitus. It is especially useful in cases of insulin resistance & oral anti-diabetic failure. It can be used singly or in combination with other oral anti-diabetic drugs for smoother control of diabetes. KARNIM is also useful for obese diabetics in whom sulfonyl ureas are contraindicated.

DOSAGE:
One capsule two time a day for freshly diagnosed non-complicated diabetes.
One capsule three times a day for cases of other oral hypoglycemic failure & insulin resistance.

ADVERSE REACTIONS:
KARNIM does not produce side effects such as nausea, vomiting, diarrhoea, rash & giddiness.

PRECAUTIONS:
Strict dietary control & a regular exercise regimen must accompany KARNIM therapy. Regular monitoring of blood sugar levels is necessary.

PRESENTATION:
Pack of 100 capsules & 15 blister strips.

KARNIM®

KARNIM is a combination of proven anti-diabetics fortified with potent Immunomodulators, Antihyperlipidemics, Anti-stress & Hepatoprotectives of total plant origin. The formulation of KARNIM is based on ancient ayurvedic references, further corroborated through modern research & clinical trials at major medical institutes.

KARNIM - A UNIQUE REMEDY

- KARNIM acts on different sites in different ways to effectively control factors & pathways leading to Diabetes Mellitus. Synthetic anti-diabetics act on one site in only one way.
- KARNIM is the only drug to correct the cause as well as effects, besides the condition itself. It attacks the various factors which precipitate the diabetic condition & corrects the degenerative complications which result because of diabetes.
- KARNIM is safe & effective in managing Diabetes Mellitus as a single agent supplement to synthetic anti-diabetic drugs.
- KARNIM helps overcome resistance to oral hypoglycemic drugs when used as adjuvant to cases of uncontrolled diabetes.
- KARNIM confers a sense of well-being in patients & promotes symptomatic relief of complaints like weakness, giddiness, pain in legs, body ache, polyuria & pruritis.

MANAGEMENT OF DIABETES USING KARNIM

KARNIM is a specially formulated capsule containing ingredients that directly or indirectly contribute in controlling diabetes. A combination of herbal drugs (see Table 1) with varying modes of action, KARNIM exerts its anti-diabetic activity in several ways.

TABLE 1 : KARNIM - ITS COMPOSITION

INGREDIENTS	QUANTITY / CAPSULE
Momordica charantia (Karela)	150 mg.
Azadirachta indica (Neem)	75 mg.
Ocimum sanctum (Tulsi)	75 mg.
Picrorhiza kurroa (Kutki)	35 mg.
Zingiber officinale (Sounth)	30 mg.
Pure *Commiphora mukul* (Shudha Guggul)	35 mg.

KARNIM®

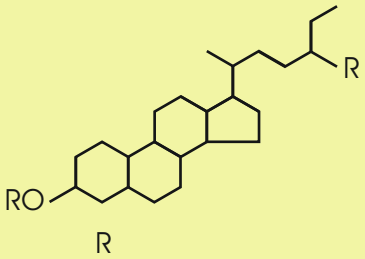
INDIVIDUAL MONOGRAPHS ON CONTENTS OF KARNIM

Momordica charantia (KARELA)

Popularly called by researchers as 'Plant Insulin'. *M. charantia* has been so named because the fruit contains a polypeptide made of 17 amino acids out of which 16 are similar to crystalline insulin of bovine origin[1,2] which has also been found to be effective in clinical trials in primary diabetes[3,4]. Understandably most of the anti-diabetic actions of *M. charantia* are insulin-like[5], due to polypeptide & charantin:

- Decreases glycogenolysis.
- Decreases gluconeogenesis.
- Retards proteolysis & promotes protein synthesis.
- Retards lipolysis & promotes storage of fatty acids Thus, *M. charantia* exerts its corrective influence in controlling diabetes by normalising the insulin deficiency status.

An alternative hypothesis suggests the mediation of anti-diabetic action of *M. charantia* through its role as a potent scavenger of superoxides & hydroxyl radicals. These radicals have been clearly indicated as causative factors of the diabetic condition[6]. indeed, the body itself possesses enzymes such as a superoxide dismutase which routinely protect the B-cells in pancreas through their scavenging action[7,8,9]. The free radical scavenging anti-diabetic role of *M. charantia* suggests an additional prophylactic role as many diabetogenic chemicals like alloxan, streptozotocin, pyrinuron, food nitrosoamines, cyanogenic glycosides such as linarnarin[10,11] & other sources of dietary cyanide induce diabetes through damage to pancreatic B-cells via free radical generation [12].



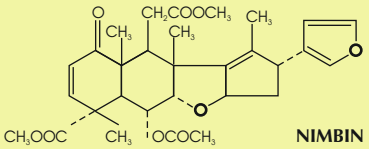
I	$-CH(CH_3)_2$	B-D-glucoside
II	$-(CH_3)C=CH_2$	B-glucosyl

B-sitosterol B-D-glucoside (1) and a new 5,25-stigmastadiene - 3-B-ol-B-D- glucoside (II) named as Charantin.

Azadirachta indica (NEEM)

A widely used drug in Ayurveda, gaining ever-growing popularity in modern times. *A. indica*, the next important ingredient in KARNIM shows its anti-diabetic action by stimulating the insulin secretion by the B-cells of Islet of Langerhans of the pancreas in a manner similar to the sulfonylureas like chlorpropamide[5].

One of the active principles is Nimbin. Besides correcting diabetes by increasing the insulin levels in blood circulation, *A. indica* also normalizes the body's immune system[13] that deteriorates in diabetic conditions due to loss of body proteins[12].

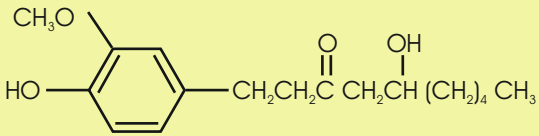


NIMBIN

***Zingiber officinale* (SOUNTH)**

Like *A. indica*, the therapeutic role of *Z. officinale* in diabetes is bivariant. Its primary action in treating hyperglycemia is mediated through its stimulatory effect on B-cells to secrete insulin. This action has been attributed to 6, 8 & 10 gingerols present in *Z. officinale*. which are assumed to cause inhibition of Na^{+}/K^{+} pump[14]. Reduced potassium conductance causes membrane depolarisation & influx of Ca^{++} ions through voltage sensitive Ca^{++} channels which ultimately stimulates insulin secretion by B-cells of pancreas.

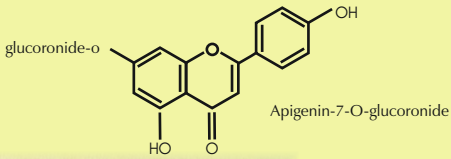
In addition to increasing blood insulin levels, *Z. officinale* has a secondary influence in lowering lipid levels in blood[15]. Elevated fatty acid levels in diabetes is a common feature due to increased lipolysis which is taken care by *Z. officinale*. Hence, it acts to prevent the onset of atherosclerosis, one of the major complications in diabetes.



***Ocimum sanctum* (TULSI)**

0. sanctum promotes uptake of glucose by peripheral tissue most likely either by decreasing peripheral resistance to insulin or any other action finally resulting in promotion of insulin: receptor interaction. This accounts for the finding that it potentiates the action of all medicaments including exogenously injected insulin[16], *M. charantia* & *A. indica*[5]. Stress is known to be a causative factor of diabetes.

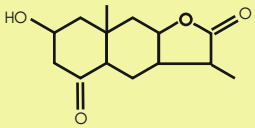
Several states of physical stress such as acute myocardial infarction, surgery, infections & severe burns & trauma associated with glucose intolerance induced by hormonal effects on glucose metabolism & insulin secretion & action[12]. Aggravation of hyperglycemia precipitated by stress is effectively taken care by *0. sanctum* which is known to possess anti-stress activity. It normalizes the stress induced neurohumoral changes[17,18].



Apigenin-7-O-glucoronide

PURE *Commiphora mukul* (GUGGUL)

One of the major complications of untreated or under treated diabetes is elevated levels of very low density lipoproteins (VLDL) in blood circulation. The VLDL is converted in the liver to more cholesterol rich low density lipoproteins that accumulate progressively on the mucosal lining of blood capillaries with subsequent narrowing of the vessel lumina. These pathological changes contribute to one of the major complication of diabetes-premature atherosclerosis. The situation may be more serious in obese patients in whom triglyceride levels are abnormally elevated.



Commiferin

C. mukul contained in KARNIM capsules is a well known anti-cholesteremic, antihyperlipidemic[28,29] agent which effectively prevents capillary thickening & subsequent pathological consequences in diabetes[29] This effect of *C. mukul* coupled with its fibrinolytic activity also prevents retinopathy, neuropathy &

gangrene which are secondary to atherosclerosis & precipitated when already narrowed blood vessels are blocked by blood clots (fibrin). One of the active principles in *C. mukul* is commiferin.

***Picrorhiza kurroa* (KUTKI)**

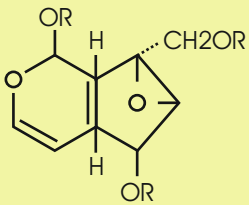
The main action of *P. kurroa* in treating hyperglycemia is attributed to the bitter principles, kutkin contained in the roots. These bitter principles are known to stimulate secretion of gastrin, secretin & chotecystokinin pancreozymin which then stimulate the secretion of insulin by B-cells of pancreas[19].

The secondary influence of *P. kurroa* in correcting diabetes is by its action as an immunomodulator by the iridoid glycoside fraction which increases the body's lowered immunity[20,21].

Liver plays a key role in a number of bodily functions. One of the more important roles of liver is maintaining a normal blood glucose concentration by controlling glycogenesis & glycogenolysis. Normal functioning of the liver is therefore extremely essential in maintaining glucose homeostasis in the body. Dysfunctioning of liver may lead to greatly altered carbohydrate & hence glucose metabolism. In such circumstances, a hepatoprotective & corrective agent is also required to restore normalcy of liver function especially if the patient is diabetic. *P. kurroa* exerts its hepatoprotective & corrective actions due to its glycosides, picrosides I & II[22,23]. These glycosides have been proved to be useful in regulating liver functions & thus, could be beneficial indirectly in controlling diabetes. It is noted that reduction of liver glycogen is the prominent feature of hepatotoxicity. The disappearance of glycogen from the liver is either due to increased glycogenolysis or due to interference in glycogenesis.

Whatever may be the mechanism of glycogen disappearing from the liver, the result obtained clearly indicates that treatment with *P. kurroa* results in accumulation of glycogen in the liver[24].

Sulfonyl urea such as glibenclamide are known to precipitate cholestasis during diabetes therapy[25]. It may be followed by jaundice[26]. Adjuvant therapy with KARNIM provides protection & prevents such toxic influence of allopathic anti-diabetics. *P. kurroa*, a component of KARNIM is known to induce bile secretion"& thus prevents cholestasis.



GLYCOSIDES	R	R'	R''
Picroside I	H	H	Glu-(6'-Cinnamoyl)
Picroside II	Vanilloyl	Glucose	H
Picroside III	H	Glu-(6'-Feruloyl)	H
Kutkoside	H	Glucose	Vanilloyl

KARNIM®

COMBINED EFFECTS OF INGREDIENTS OF KARNIM

In a study, *M. charantia*, *A. indica* & *O. sanctum* in combination showed inhibitory effects on enhanced gluconeogenesis from proteins & amino acids with the accumulation of glycogen in liver. Ultimately, blood glucose level reduced significantly & remained maintained till the termination of the drug[5]. KARNIM, as a complete prescribed formulation produces highly significant reduction in blood glucose level progressively improving up to the end of months[31] (see fig. 1).

KARNIM also reduces different symptoms associated with diabetes[31] (see fig. 2).

Addition of KARNIM after one month to the therapy of glibenclamide, caused a further reduction of blood sugar level by 26.7% in fasting blood sugar & by 44.21% in post-prandial blood sugar, during the second month[31] (see fig. 3,4).

Fig. 1: Monthly actual mean values of Blood sugar with KARNIM for 3 months

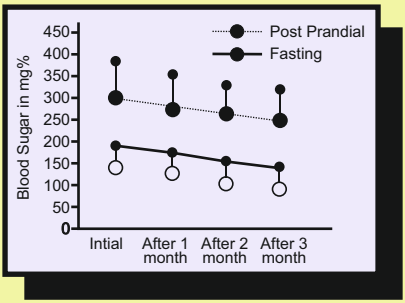


Fig. 2: Relief in Symptoms with KARNIM

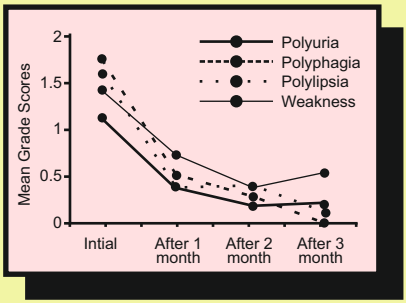


Fig. 3: Increasing response of KARNIM (mean blood sugar reduction in mg % monthwise)

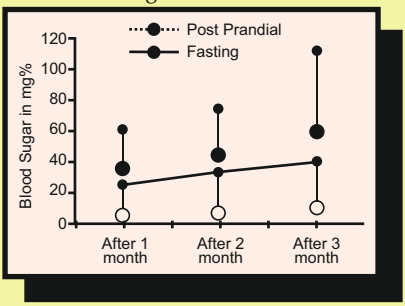
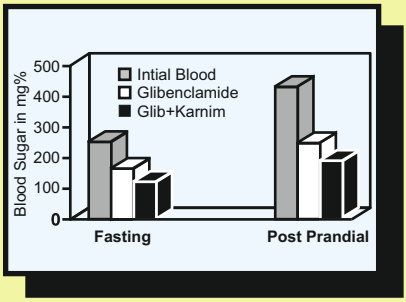


Fig. 4: KARNIM's potentiation effect of Hypoglycemics of Glibenclamide



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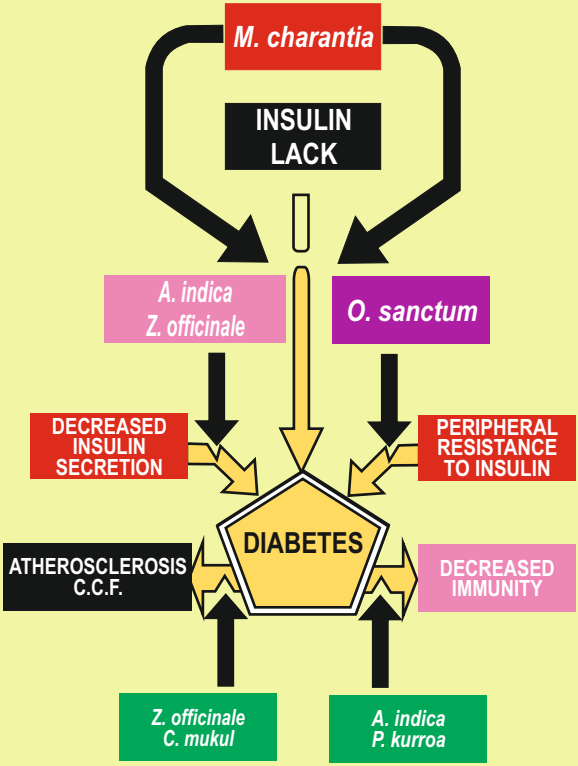
THERAPEUTIC EFFECTS OF KARNIM



PATHOPHSIOLOGICAL CHANGES IN DIABETES	CORRECTIVE EFFECTS OF KARNIM INGREDIENTS
Lack of insulin.	*M.Charantia* normalizes the deficiency status.
Decreased secretion of insulin.	*A.indica* & *Z.officinale* stimulate Bcells of pancreas to secrete insulin.
Increased peripheral resistance to circulating insulin.	*O.sanctum* decreases peripheral resistance & promotes insulin receptor interaction.
Increased risk for atherosclerosis & subsequent congestive	*Z.officinale* & *C.mukul* prevent narrowing of vessels by lowering systemic levels of cholesterol & free fatty acids.
Decreased immunity due to proteolysis	*P.Kurroa* & *A.indica* normalize the body's immune system.

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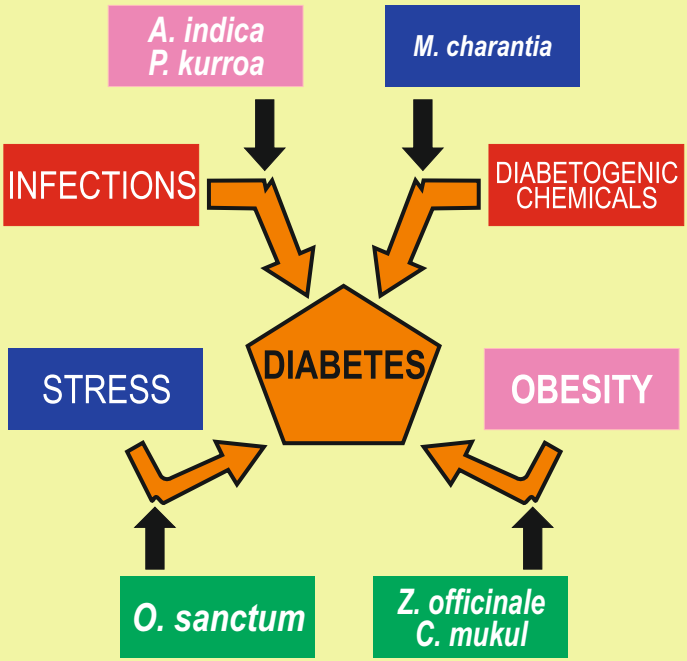
PROPHYLACTIC ROLE OF KARNIM



ETIOPATHOGENESIS OF DIABETES	PROTECTIVE INFLUENCE OF KARNIM CONTENTS.
Infections	*A. indica* & *P.kurroa* increases the body's resistance to infections including those of viral origin.
Diabetogenic chemicals	*M.Charantia* protects the B cells from the cytotoxic action of superoxide & hydroxyl radicals by its scavenging actions
Stress (Physical & emotional)	*O.sanctum* normalizes stress induced neurohumoral changes which may otherwise precipitate diabetes.
Obesity & over nutrition	*Z.officinale* & *C.mukul*'s antihyperlipidemic action decreases accumulation of body fats & subsequent peripheral resistance to insulin which, if persist for long, may precipitate diabetes.

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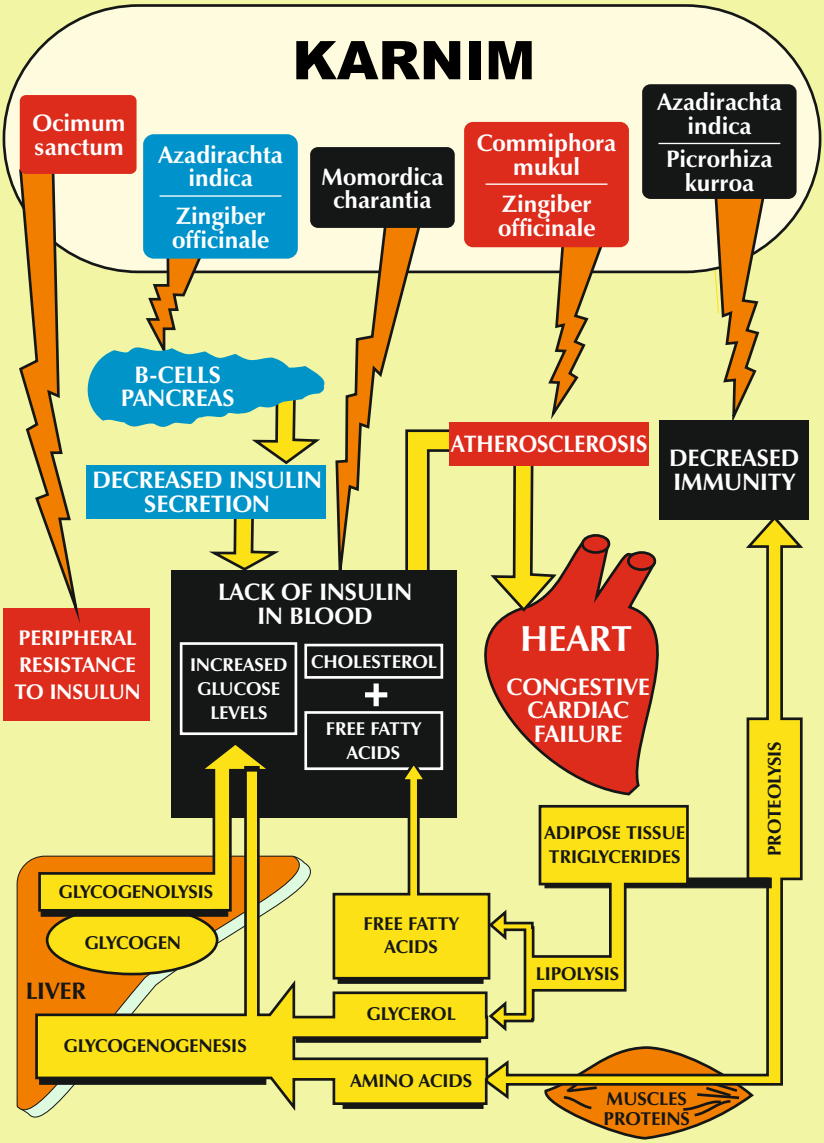
THERAPEUTIC ROLE OF KARNIM IN DIABETES MELLITUS



BIOCHEMICAL AND PATHOLOGICAL CHANGES IN DIABETES MELLITUS

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FOR MEMBERS OF THE MEDICAL FRATERNITY & DIABETIC PATIENTS

KARNIM is purely a herbal remedy formulated after extensive research & clinical trials in major medical institutes, which is accepted worldwide in over 14 countries. It acts as a supplement to oral hypoglycaemics & insulin when diabetes is not controlled. It arrests complications arising due to uncontrolled diabets which affect the heart, eyes, kidneys & nerves. It is free from side effects due to its herbal origin, thus instilling a sense of well-being in the patient. Enabling diabetics worldwide to lead normal lives. Available at all leading chemists, in pack of 100 capsules.

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