In this issue:

1. Acarbose, an update of its therapeutic use in diabetes treatment. (page 1)
2. Long-term improvement of metabolic control by Acarbose in type-2 diabetes patients poorly controlled with maximum sulfonylurea therapy. (page 3)
3. Safety and tolerability of Acarbose in treatment of type 1 and 2 DM. (page 5)
4. Initiating and Intensifying Insulin therapy for type-2 DM: Why, when, and how. (page 6)
5. Addressing barriers to insulin therapy: the role of Insulin pens. (page 9)
Acarbose
An Update of Its Therapeutic Use in Diabetes Treatment.

Heiner Laube, Department of Internal Medicine, Universität Giessen, Giessen, Germany. Clin Drug Invest 2002; 22 (3): 141-156, 1173-2563/02/0003-0141

Oral antidiabetic drugs are becoming increasingly important as rates of type 2 diabetes, uncontrolled by dietary intervention alone, increase around the world. Therapeutic agents that target the early stages of type 2 diabetes, such as the α-glucosidase enzyme inhibitor acarbose, which reduces postprandial hyperglycaemia and hyperinsulinaemia, now have a more prominent role to play in diabetes management in view of increasing evidence that the postprandial state is an important contributing factor to the development of atherosclerosis. This review provides an update on the role of acarbose in present day diabetes care. Acarbose is a first-line treatment for newly diagnosed patients with type 2 diabetes, those who have high postprandial blood glucose and for patients where dietary treatment alone provides inadequate glycaemic control. Acarbose lowers blood glucose when administered as monotherapy and in combination with other oral antidiabetic drugs. It reliably reduces levels of glycated haemoglobin (HbA1c) and also increases insulin sensitivity; however, unlike insulin and the sulphonylureas, acarbose has not been associated with bodyweight gain. The aim of this review is to present clinical data on the pharmacology and efficacy of acarbose in the treatment of patients with type 2 diabetes mellitus. It is not intended to present a comprehensive review of the treatment of diabetes mellitus in general. In these patients, acarbose can lower postprandial blood glucose significantly by over 2.7 mmol/L and decrease HbA1c level by up to 0.8 to 1.0%. In patients with type 2 diabetes with fasting hyperglycaemia above 11.0 mmol/L, acarbose may be combined with other well-established anti-hyperglycaemic agents, resulting in an additional lowering of HbA1c.

Effects on Lipid and Lipoprotein Metabolism: Treatment with acarbose is associated with several changes in lipid profile. Serum triglycerides, very low-density lipoprotein (VLDL) concentration and free fatty acids are frequently elevated in obese patients with insulin-resistant type 2 diabetes. Several studies have documented a dose-dependent reduction in blood lipids with acarbose in this patient population.
Effect on Blood Pressure: In overweight patients with type 2 diabetes and mild hypertension, acarbose lowers systolic blood pressure (5.2 ± 2.4 mm Hg) significantly (p = 0.0001) after 24 weeks and decreases heart rate slightly compared with glibenclamide. These effects can be explained by the lower insulin levels following acarbose treatment, which, in turn, reduce sympathetic nervous system activity and insulin-induced vasodepressor action.

Effect on Coagulation: In 17 patients with type 2 diabetes maintained on diet therapy alone who consumed a standard meal (372 kcal, 49% carbohydrate, 40% fat, 11% protein), a single dose of acarbose 100mg significantly attenuated the postprandial rise of prothrombin fragments 1 and 2 (2.0 vs 2.7 mmol/L, at 2 hours) and D-dimer (2.85 vs 3.50 g/L, at 1 hour) compared with placebo. These components are sensitive markers of ongoing coagulation activation and fibrinolysis. Prothrombin fragments 1 and 2 have been shown to be strong predictors of thrombotic coronary stent occlusion, and D-dimer, a primary degradation product of cross-linked fibrin, is a predictor of myocardial infarction. Thus, acarbose may be useful in reducing meal induced activation of haemostasis in the procoagulative state of diabetes mellitus.

Comment:
Nearly 285 million people worldwide, with 10% being Americans, suffer from diabetes mellitus and its associated comorbidities. This is projected to increase by 6.5% per year, with 439 million inflicted by year 2030. Both morbidity and mortality from diabetes stem from the consequences of Microvascular and macro vascular complications. The global prevalence of type 2 diabetes continues to increase at an alarming rate. The number of patients with type 2 diabetes is estimated to rise from 150 million affected individuals worldwide today to 300 million within the next 25 years. Consequently, the burden of diabetic microvascular complications, cardiovascular disease and the costs of treatment are set to increase dramatically as type 2 diabetes becomes more prevalent. Acarbose binds reversibly, competitively and in a dose-dependent manner to the oligosaccharide binding site of α-glucosidase enzymes in the brush border of the small intestinal mucosa. As a consequence, hydrolysis is prevented. This effect lasts for 4 to 6 hours provided that acarbose is present at the site of enzymatic action at the same time as the oligosaccharides. Thus acarbose must be administered with the first bite of a main meal. Lowering of total serum triglycerides is primarily mediated via a reduction in the biosynthesis of VLDL and is secondary to acarbose-induced attenuation of postprandial hyperinsulinaemia. At present, 1.9 million diabetic patients have been treated with α -glucosidase inhibitors worldwide. The Cochrane Library lists 143 published placebo-controlled trials that have evaluated the efficacy of acarbose on HbA1c and fasting and postprandial blood glucose. All identify a significant improvement of metabolic control following acarbose in patients with type 2 diabetes mellitus. These studies include patients controlled by diet alone and patients who received additional oral antihyperglycaemic agents and insulin.
An interaction between digoxin and acarbose was reported in two patients with congestive heart failure. Addition of acarbose resulted in sub-therapeutic digoxin plasma concentrations. Acarbose does not interfere with the absorption of sulphonylureas, ACE inhibitors, β-blockers or warfarin. More recent studies have confirmed additional glycaemic control in diabetic patients when acarbose is co-administered with metformin.

Acarbose should be withdrawn in cases of progressive renal insufficiency (serum creatinine>3.5 mg/dl). Few data exist for this patient group and there is limited experience to confirm whether acarbose metabolites accumulate in the plasma. Acarbose is antihyperglycaemic rather than hypoglycaemic. Acarbose use is appropriate in elderly patients with type 2 diabetes, where asymptomatic hypoglycaemic reactions are potentially dangerous. Acarbose does not cause bodyweight gain; use is therefore appropriate in obese diabetic patients. In subjects with impaired glucose tolerance, acarbose increases insulin sensitivity up to 30%, suggesting that the drug may have a preventive role in the progressive transition to overt type 2 diabetes. Clinical trials to investigate this potential are ongoing.

2. Long-Term Improvement of Metabolic Control by Acarbose in Type 2 Diabetes Patients Poorly Controlled with Maximum Sulfonylurea Therapy


This study investigated the addition of acarbose to maximum doses of sulfonylurea in very poorly controlled type 2 diabetes patients and assessed its effect in delaying further glycaemic deterioration. In this 78-week, double-blind, placebo-controlled European study, patients were randomised to receive acarbose, titrated to a maximum dose of 100mg three times daily, or matching placebo. Concomitant sulfonylurea treatment (glibenclamide/gliclazide) was to remain unchanged throughout the study. A sample size of 171 patients per treatment arm was calculated. The primary efficacy analysis was intention to treat. The change in glycosylated haemoglobin (HbA 1c ) levels from baseline to the end of the study was regarded as the primary efficacy variable. Patients whose HbA 1c  levels increased above 10.5% on two consecutive visits terminated the study prematurely because of insulin administration. Secondary efficacy variables included the changes in blood glucose and C-peptide, both at fasting and at the 1h-postprandial level. A total of 330 patients (acarbose 164, placebo 166) were valid for the efficacy analysis. Patients were generally overweight (body mass index 29.0 kg/m2) and showed very poor metabolic control (HbA1c >9%, fasting blood glucose>200 mg/dL, and 1h-
postprandial blood glucose >300 mg/dL). Acarbose significantly improved HbA1c levels compared with placebo (least square mean [LS-mean] difference –0.54%, 95% CI –0.86 to –0.22; p =0.001). A number of patients had to discontinue the study prematurely because of insulin administration (24.5% in the placebo and 14.2% in the acarbose group). There was a significant LS-mean difference of –14.8 mg/dL (p = 0.0195) in fasting blood glucose levels and highly significant differences in 1h-postprandial blood glucose (LS-mean difference –33.4 mg/dL, p < 0.0001) and in the rise in blood glucose from fasting to 1h postprandial (LS-mean difference –19.6 mg/dL, p = 0.0001), all in favour of acarbose. Acarbose was shown to have a good safety profile and was generally well tolerated. Conclusion: Acarbose has been shown to be efficacious as add-on therapy to maximum sulfonylurea treatment in a patient population with highly inadequate glycaemic control. The addition of acarbose resulted in a mean HbA 1c reduction of 0.42%. Furthermore, optimal metabolic control (HbA 1c <7%) was achieved in 11% of the acarbose recipients. The efficacy of acarbose might be explained by its mode of action, which leads to a reduction in postprandial hyperglycaemia a reduction that has been shown to be important for the delay of progression of type 2 diabetes. The recent results of the Study TO Prevent Non-Insulin Dependent Diabetes Mellitus (STOP-NIDDM) trial also underlined the efficacy of acarbose in delaying type 2 diabetes development, and development of cardiovascular events in patients with impaired glucose tolerance. A meta-analysis of seven placebo-controlled acarbose studies confirmed the effect on cardiovascular events in patients with type 2 diabetes.

**Comment:**
This study confirms the finding that glycaemic control can still be improved in very poorly controlled subjects who do not want or cannot be put on insulin treatment. On the basis of the presented data it can be assumed that further improvements might be seen in the present study population under clinical practice conditions where acarbose is titrated to the patient’s individual needs. The difference in the rise in blood glucose from fasting to 1h postprandial is -18.6 and not -19.6 as mentioned in the paper. This has recently been demonstrated in a 5-year surveillance study: sulfonylurea-treated patients showed considerable improvement in HbA1c (~2%), fasting blood glucose (~50 mg/dL) and 2h-postprandial glucose (~63 mg/dL) with long term acarbose treatment. When interpreting the data from the present study, one has to bear in mind that diabetes treatment has undergone considerable changes since the early 1990s when this study was planned. Indeed, the present trial was carried out from July 1996 to November 1999 and the data analysis took place in 2000. The results of the UKPDS (UK Prospective Diabetes Study) have led to new recommendations concerning HbA1c levels in type 2 diabetes patients, Insulin treatment has to be initiated at a much lower level than 10 years ago. The European Diabetes Policy Group suggests starting insulin therapy when HbA1c has deteriorated to >7.5% after maximum attention to dietary control and oral glucose-lowering therapy. HbA1c levels of the patients included in this study were much higher (8.5–10.5%) than would be accepted today. The data presented here, however, show that even very poorly controlled patients can benefit from the addition of acarbose.
3. Safety and Tolerability of Acarbose in the Treatment of Type 1 and Type 2 Diabetes Mellitus


The objective of this study was to assess the safety profile of acarbose treatment over a 1-year period at a dose range of 50–300mg three times daily in patients with type 1 or type 2 diabetes mellitus. In this 56-week, double-blind, parallel-group, multicentre comparison, patients were randomised to acarbose or placebo in a 2 : 1 ratio. An 8-week forced titration phase (from 50–300mg three times daily) was followed by a 48-week maintenance phase during which patients received the highest dose tolerated during titration. Patients were assessed at 13 visits with respect to adverse events/intercurrent illnesses, abnormal laboratory values (serum chemistry, urinalysis, complete blood and reticulocyte count, serum iron and total iron binding capacity, and serum vitamin B6, B12, D and folate levels), discontinuation rates, ECG findings, vital signs and evaluation of the patients’ diaries with regard to gastrointestinal events. A total of 359 patients (acarbose 240, placebo 119) were valid for analysis; 21% had type 1 diabetes. Most patients received concomitant insulin or sulfonylurea treatment. Study withdrawal was reported for 35% of acarbose and 24% of placebo recipients (p = 0.053); adverse events were the main reason for withdrawal in acarbose recipients (20%; placebo group 5%; p < 0.01). The most common adverse events for acarbose recipients were gastrointestinal (abdominal pain, flatulence and diarrhoea), which were more frequent than in placebo patients (p< 0.01). These events occurred more often early in the study and attenuated over time. It was concluded that The majority of type 1 or type 2 diabetic patients tolerated acarbose well during the 1-year treatment period despite use of a very high dosing regimen. Gastrointestinal adverse effects attenuated over time and no new clinically significant safety concerns for acarbose were identified.

Comment:
Acarbose was well tolerated by the majority of patients in spite of the very high dosing regimen used. The most common events in the acarbose group were gastrointestinal problems. Abdominal pain, diarrhea and flatulence all occurred more often and were more moderate or severe in intensity. There was also an increase in bowel movements and in the occurrence of unformed and soft or watery stool. These symptoms are directly related to the drug’s mechanism of action and are caused by inhibition of carbohydrate digestion in the small intestine. This can lead to the delivery of undigested carbohydrates into the large intestine where microorganisms ferment them into short-chain fatty acids, methane, carbon dioxide and hydrogen. This can cause abdominal discomfort, increased flatulence and loose stool. Gastrointestinal events occurred more frequently early in the Study and attenuated over time.
4. Initiating and Intensifying Insulin Therapy for Type 2 Diabetes: Why, When, and How:

Michael E. Cobble, MD, Canyons Medical Center, Sandy, UT. American Journal of Therapeutics 16, 56–64 (2009).

With the exception of insulin, all diabetes medications have limited glucose-lowering capacity. Therefore, as type 2 diabetes progresses, insulin is often needed to achieve near-normal glycaemic targets and avoid complications. Concerns about the initiation of insulin by both clinicians and patients play a major role in poor glycaemic control. This article discusses current guidelines for treating type 2 diabetes, exploring when and how insulin therapy should be initiated and intensified, and how barriers to insulin use may be overcome. To help achieve A1C targets, the ADA (American Diabetes Association) has developed a consensus algorithm for the initiation and intensification of therapy, and the ACE/AACE (American College of Endocrinology / American Association of Clinical Endocrinologists) has provided extensive therapeutic guidelines and “road maps” for the prevention and treatment of type 2 diabetes. Advances include the development of novel long-acting, premixed, and rapid-acting insulin analogues and delivery devices. These agents have near-physiological time–action profiles that allow safer, flexible, and more convenient dosing.

Insulin pumps are programmable devices, no bigger than a pager, holding an insulin reservoir, and use a single type of insulin typically a rapid-acting insulin analogue —to closely mimic natural insulin physiology and to meet both prandial and basal requirements. Use of an insulin pump allows patients to avoid multiple daily injections. Insulin pumps are highly effective at achieving and maintaining stringent A1C targets, which may offset the higher cost of these devices. Many patients find using an insulin pen device easier, more convenient, and more discreet than using a vial and syringe. Nurses and medical assistants can be trained to understand the glucose-lowering capacities and limitations of each class of diabetes medications, including recognizing when insulin therapy is necessary. In addition, by showing patients how easy insulin pens are to use, clinic staff can help empower, educate, and encourage patients with type 2 diabetes to optimize their glycaemic control with insulin once oral antidiabetic agents alone have become inadequate. Type 2 diabetes is highly variable in presentation, and therapy relies heavily on the experience of the clinician in identifying the right combination of lifestyle and pharmacological interventions for each patient. Simple and effective regimens have been identified for initiation of insulin therapy, such as adding newer long-acting analogues of insulin to established oral medication, or the use of premixed insulin analogue just before meals. Basal insulin is most effective for fasting glucose control, bolus insulin for meal time prandial control. Premixed insulin preparations may effectively target both glucose issues. Starting insulin at 0.2 units/kg/d and titrating rapidly (every 1–2 days) to achieve FPG and PPG goals (shared with the patient) empowers and involves the patient and has been shown to be effective and safe in glycaemic control. The following table shows the expected A1C decrease with antidiabetic agents.
Comment:

Multiple studies have shown that failure to achieve glycaemic targets over time occurs in the absence of insulin initiation. The traditional approach, in which insulin was an agent of last resort, is being replaced by a more progressive approach to preempt morbidity and mortality. Ultimately, insulin is, and should be, a cornerstone treatment for those patients not achieving adequate glucose control within 3–6 months. Insulin use should be embraced in our primary care practices and not viewed as a punishment, highly complicated or an end-stage treatment option. In our clinic, we aim to help patients understand that insulin replacement is normal and healthy. It is particularly important to start insulin before multiple organ failures occur, such as those involving cardiac, cerebral, renal, pancreatic, retinal, and peripheral vascular systems. Insulins of today make using insulin so much easier than the insulins 20 years ago. Use of insulin pens can help facilitate stringent glycaemic control and also help empower and encourage patients. With the right approach, patients will find that glucose control can be achieved effectively and that insulin is a healthy and natural addition to glucose management.
Table 3. Mnemonics defining goals of patient management for type 2 diabetes for all patients aged 40 years or older unless contraindicated or special circumstances.

<table>
<thead>
<tr>
<th>L</th>
<th>LDL cholesterol &lt;70–100 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A1C &lt;7%</td>
</tr>
<tr>
<td>B</td>
<td>Blood pressure (systolic) &lt;120–130 mmHg</td>
</tr>
<tr>
<td>S</td>
<td>Statin treatment; systolic blood pressure control</td>
</tr>
<tr>
<td>U</td>
<td>Urine microalbumin testing annually, and correction if above normal limits</td>
</tr>
<tr>
<td>G</td>
<td>Glucose:*</td>
</tr>
<tr>
<td></td>
<td>FPG &lt;90–130 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Postprandial plasma glucose &lt;140–180 mg/dL</td>
</tr>
<tr>
<td></td>
<td>A1C &lt;7%</td>
</tr>
<tr>
<td>A</td>
<td>ACE inhibitor treatment; acetylsalicylic acid treatment</td>
</tr>
<tr>
<td>R</td>
<td>Retinal exam annually</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; LDL, low-density lipoprotein. For treatment of specific patient groups, including the elderly, pregnant patients, and those aged younger than 40 years with overt cardiovascular disease or multiple risk factors, see Ref. 15. *These are crucial glycemic goals and if not achieved within 3–6 months of treatment with oral antidiabetic drugs, initiation of insulin treatment should be strongly considered.

American Journal of Therapeutics (2009) 16(1)
5. Addressing Barriers to Insulin Therapy: The Role of Insulin Pens

Melissa L. Magwire, RN, CDE. Shawnee Mission Medical Center, Shawnee Mission, KS. American Journal of Therapeutics 18, 392–402 (2011)

Despite the fundamental role of insulin therapy in diabetes management, many patients and some clinicians may resist insulin initiation due to concerns about its complexity or a general resistance to injections. Many patients’ concerns about insulin initiation may stem from perceptions about the pain and inconvenience of using vials and syringes for delivering insulin. However, insulin pen devices offer an easier method for insulin administration that is more accurate, less painful, their small size, portability, and more discreet compared with vials and syringes. Advances in insulin pen technology have enhanced their utility by increasing their accuracy, reducing the injection force required, and incorporating mechanisms to store the dose, time, and date of previous insulin injections.

Preferences for insulin delivery devices:

Substantial evidence demonstrates that insulin pen devices are preferred by both patients and clinicians and have the potential to improve adherence, enhance quality of life, reduce the risk of hyperglycemia, and decrease costs. Ultimately, the advantages of insulin pens may reduce resistance to initiating and adhering to insulin therapy. Because insulin pens are underused in the United States compared with in other countries, it is critical that clinicians understand the potential benefits of insulin pens and communicate them to their patients. Clinical studies have demonstrated that insulin pen devices provide increased ease of use and convenience, improved flexibility, greater accuracy, enhanced QOL, increased perceived efficacy, and greater social acceptability compared with the vial and syringe. These benefits have been reported in patients previously naive to insulin therapy, in children, in the elderly, and in patients with impairments in vision or dexterity. Reducing the burden of treatment with more convenient insulin delivery systems, such as insulin pen devices, could help patients achieve improved diabetes outcomes.
**Comment:**

With the recent enhancements to the design and performance of insulin pens, it is expected that prefilled insulin pens may become the most widely used method of insulin delivery. Clinicians who care for patients with diabetes, patients with diabetes, and payers should help reduce barriers to insulin initiation by incorporating insulin pen devices into treatment recommendations and diabetes management programs and protocols.

One of the most common barriers to the adoption of insulin pen devices in the United States is a concern about their cost. Although the costs of insulin pen devices may be higher than those associated with vials and syringes, evidence suggests that total annual treatment costs may be reduced. In one study, total annual treatment costs, including the cost of the insulin delivery device and the insulin, were reduced by $1590 per patient among those who switched over to pen use. The authors reported that reductions in costs resulted from reduced hypoglycemia-attributed Costs (e.g. costs related to hospitalization, emergency department visits, and physician visits) and other costs attributable to diabetes care. This study also reported a reduction in overall diabetes-related pharmacy acquisition costs due to reductions in the cost of oral antidiabetic agents, a finding that could reflect improved self-management and enhanced glycaemic control, which may have led physicians to reduce the number, strength, or daily dose of oral agents. In addition, overall insulin costs remained the same among individuals who switched over to the pens and those who continued using the vial and syringe, despite the higher costs of the insulin analog pen devices. This finding may have resulted from improvements in adherence that may have allowed for the use of lower daily doses of insulin or from reductions in wasted insulin with pens compared with vials and syringes due to the expiration of insulin in vials. Another study in a Medicaid population reported that total annual healthcare costs were 50% less among patients who initiated insulin using pen devices compared with those who started therapy with the vial and syringe; however, no cost savings were reported among patients who switched from the vial and syringe to the pen. Insulin prescription costs among patients who initiated therapy with insulin pens were also significantly lower than costs among patients initiating therapy with vials and syringes. Introducing patients to insulin pens in the hospital may facilitate insulin use after discharge in patients who require insulin therapy.

The treatment cost comparison between insulin delivery pen devices and insulin delivered in vials and syringes more future studies and clinical trials are required.
General evaluation of paper literature:
Author: Many authors of different setting, institution, educational facilities, organizations, countries, etc, that guarantees there is no commercial sponsoring (except for two review articles regarding insulin No. (5) and No. (6) which are supported by some multinational pharmaceutical companies) and this means clinical trials are well controlled and neutral even some are lacking statistician.
Introduction should provide a brief pharmacotherapy literature of acarbose and insulin therapy such as: mode of action, clinical indications, efficacy, toxicity, monitoring parameters, etc.
Methodology: the review and original articles provide criteria of selection, inclusion, and exclusion of population.
Conclusion: the review authors and original article authors are directly come to conclusion of published papers of therapeutic trials. All identity, a significant improvement of metabolic control, following acarbose in patients with type-2 diabetes mellitus. But clinical trials to investigate this are ongoing. The treatment cost comparison between insulin delivery pen devices and insulin delivered in vials and syringes more future studies and clinical trials are required.
Reference: extensive bibliography is listed which provide an axis to a wide selection of good relevant and updated articles.

Conclusion and recommendations: Acarbose may increase the risk of hypoglycemia when used in combination with other hypoglycaemic agents, and this may increase the effect of and toxicity. So dosage of acarbose may need to be adjusted. Dosage should be adjusted in renal impairment. Serum transaminase (LFT) should be routinely checked. Acarbose is safe in pregnancy. But blood glucose level should be checked routinely (congenital abnormalities may occur due to abnormal glucose level in pregnancy).
To initiate insulin and intensify therapy for type-2 diabetes mellitus physician should consider the mnemonic (guidelines) defining goals of patient management for type-2 diabetes mellitus for patient aged 40 years or elder to be start after 3-6 months of treatment with oral antidiabetic when they fail to achieve glycaemic control as mentioned in the American Journal of Therapeutics (2009) 16(1).
Insulin bumps are very costly, so we should think of this point and also their availability in Sudan. Insulin pen has many advantage and benefits over insulin vials and syringes (clinically, socially, etc.), but care should be taken regarding cost, availability and patient education.
Pharmacist should contribute widely in patient education and counseling particularly in treatment therapy of chronic life-long disorders (e.g. diabetes, hypertension, etc.). as those diseases need proper monitoring, follow up and updating drug information. Pharmacist should be trained and educated intensively on the clinical use of medication, in order to review the outcomes of pharmacotherapy and management of such diseases (efficacy and toxicity).
Health care providers have to know the new technology and advances of investigation and management of diseases particularly in developing countries such as Sudan.
Drug Therapy Scan

Editor: Dr. Azhari Elnour H. Elamin, B.Pharm, CHP, RPh, FSHP. Associate Professor & Consultant of Clinical Pharmacy, Hospital Pharmacy & Therapeutics, Faculty of Pharmacy – Karary University, Department of Pharmaceutical Services - Military Medical Services Administration, Sudan.

Contributor: Al-Khair Adam Khalil, B.Pharm, Faculty of Pharmacy – Karary University, Department of Pharmaceutical Services - Military Medical Services Administration, Sudan.