**Does the yellow tablet really work?**

DDB is an intermediate process of synthesizing Schizandrin C, a natural compound isolated from *Fructus schizandrae chinensis*. DDB is chemically designated as \((\text{Dimethyl-4, 4'-dimethoxy-5, 6', 6'-dimethylenedioxybi-phenyl- 2, 2'dicarboxylate})\). [1]

The DDB tablet is produced by Beijing Union Factory, Beijing, China and registered as liver support medication in China as well as in Egypt, and it is known in the latter as **(الحياة)** [2]. It is imported and distributed by Al-Ahram Pharmaceutical and Medical Equipment Company and it is widely used for the treatment of chronic liver diseases of different etiologies including Hepatitis C.

The beneficial effects of DDB have been observed in liver cell injury models (in-vitro studies or animal), which had revealed that; DDB could protect against liver injuries induced by carbon tetrachloride (CCl4), D-galactosamine, thioacetamide and prednisolone in mice and rats [2, 3, 4] also it has curative effect against tamoxifen-induced liver injury in rats. [5]

Though many Egyptian physicians would claim their good experience with this treatment, however human studies in the literatures are very scarce. In 2 Clinical trials (human studies) on chronic viral hepatitis B patients, DDB demonstrated significant improvement of impaired liver functions, such as elevated levels of alanine transaminase ALT (previously known as SGOT), bilirubin and alpha fetoprotein as well as symptoms in patients [6, 7].

In order to determine the effect of DDB (HpPro® trade name in Indonesia) on patients with acute and chronic liver diseases (Akbar N, et al, 1998) had designed 2 clinical studies; one open trial and another prospective randomized controlled study. [8]

The open trial included 56 cases (16 cases with acute hepatitis, 20 cases with chronic hepatitis, and 14 cases with liver cirrhosis and 6 cases with fatty liver) while the Controlled study consisted of 20 cases of **Child A** chronic hepatitis they were randomly treated with either DDB (HpPro) or a mixture of known drugs which used as liver protective agent in Indonesia as control for one week. The patients were then crossed over those two drugs in the next week. Results of the open trial, after 4 weeks’ treatment with DDB (HpPro) 7.5 mg orally three times daily were; Patients with acute hepatitis, chronic hepatitis and fatty liver showed rapid decrease of Aspartate transaminase (AST) and SGPT (ALT) while the patients who were liver cirrhosis cases, SGOT and SGPT were decreased slowly.

While in the controlled trial; nine patients received DDB (HpPro) 7.5 mg three times daily orally and eleven were treated with a mixture of known drugs as the controls. After one week...
treatment, DDB (HpPro) group clinically showed significant decrease of SGPT and SGOT levels compared to control group (p<0.035).

At the second week, DDB (HpPro) group showed significant decrease of SGOT compared to control group (P=0.038) however the decrease of SGPT was not significant (P=0.096).

The authors concluded that treatment with DDB (HpPro) is effective to reduce liver impairment in acute and chronic liver diseases on Indonesian patients and no side effect of DDB (HpPro) was observed.[8]

However, all above studies on human were small in number and performed over a short period of time. The efficacy of the treatment was evaluated by measuring the liver enzymes as the surrogate end points; however none of them had measured the degree of cirrhosis or the inflammation grade as an outcome for the treatment.

On the other hand a retrospective study on 13 patients (10 with chronic hepatitis C, 1 with chronic hepatitis B, 2 with nonalcoholic steatohepatitis) who were treated with DDB (12 mg, 3 times per day) in outpatient clinic of the University Hospital Freiburg, Department of Medicine II, Freiburg, Germany between 2000 and 2003. [9]

The ALT level was rapidly normalized in 12/13 patients and remained normal during treatment. However the level of the other parameters; aspartate aminotransferase, gamma-glutamyl transferase and glutamate dehydrogenase levels were not affected. Furthermore, 5 patients with chronic hepatitis C had liver biopsies after 1 year of treatment that could be compared with biopsies obtained 3–20 months before treatment. The grade of inflammation was unchanged in 2, worse in 2, and better in 1 patient; the stage of fibrosis was worse in 3 and stable in 2 patients. All 5 patients had responded to DDB treatment with a persistent ALT normalization however none of them had measured the degree of cirrhosis or the inflammation grade as an outcome for the treatment.

Conclusion:
Till we have a long-term randomized control Trial that addresses the histological benefit of DDB on Hepatoes the routine use of DDB should not be encouraged.

References:
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9. HUBER R, HODGENUS B, BLUM H E.University Hospital Freiburg Department of Medicine II Freiburg, Germany. DDB Treatment of Patients with Chronic Hepatitis. HEPATOLOGY 2004; 39:1732–1733.
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IBUPROFEN ABOLISHES THE ANTIPLATELET EFFECT OF ASPRIN:

FDA recently released an information sheet advising healthcare professionals about a potential pharmacodynamic interaction between low-dose aspirin (81 mg/d) and ibuprofen 400 mg when they are dosed concomitantly. (An interaction that was first reported in 2003). This interaction may attenuate aspirin’s anti-platelet cardio-protective effect in patients taking aspirin for secondary prevention of myocardial infarction.

Previously some epidemiologic studies had pointed toward this potential problem. An analysis of data on 7,187 patients discharged on low-dose aspirin (< 325 mg/day) after their first hospitalization for cardiovascular disease showed that; patients who were also taking ibuprofen (at mean daily doses of 1,210 mg) had a 93% increased risk of all-cause mortality and a 73% increased risk of death from cardiovascular causes, both were significant when compared with patients who were taking aspirin alone. The possible mechanism for the interference may be the competitive inhibition of the acetylation site of cyclooxygenase (COX) in the platelet. Similar interference also has been observed when a single dose of ibuprofen has been taken 8 hours before aspirin or sooner.

However occasional use of ibuprofen by patients carries a minimal risk of the interaction, that is because of aspirin’s long-lasting anti-platelet effects when taken daily. To minimize the pharmacodynamic interaction, FDA advises that patients should wait at least 30 minutes before taking ibuprofen after ingesting the immediate-release low-dose aspirin or if taking ibuprofen prior to the aspirin, patients should wait at least 8 hours before ingesting the aspirin.

References are available upon request; http://fda.gov/cder/drugs/infosh/ibuprofen_aspirin.htm
ASPIRIN AND THE ANTICANCER EFFECTS

Aspirin is a multifaceted compound, in addition to its anti-platelet, antipyretic and anti-inflammatory benefits; it may decrease the risk of colorectal neoplasia. This has been revealed from early (15 years ago) epidemiologic as well as recent clinical studies.[1-7] This protective effect is dose dependent, and more important, is directly related to the duration of exposure.[8-9]

The proposed mechanism for the protective effect is by blocking cyclooxygenase (COX) thus suppressing the levels of mucosal prostaglandins E2 and F2α in colorectal mucosa (High levels of prostaglandins are observed in colon cancer tissues) these prostaglandins play an important role in maintaining blood supply to tumors and inhibition of their production will therefore limit tumor growth.[10, 11]

Recent in-vivo and animal studies[12-14] have showed that aspirin at high doses caused death of the blood vessel cells (an effect that was not seen with standard doses of aspirin nor with Celebrex and the other NSAIDs, which largely target just cyclooxygenase), this may cause aspirin not to represent a suitable treatment for cancer.

However understanding how the drug works may lead to new therapies.

References:


CANC O2ELTAMIVIR (Tamiflu®) BE USED IN INFANTS AND NEONATES?

Oseltamivir is an oral prodrug of oseltamivir carboxylate, an inhibitor of the enzyme neuraminidase (sialidase), which has a role in the infectivity and replication of influenza A and B viruses. Oseltamivir recommended dose for the treatment of influenza in children 1 year and above is based on the body weight and is as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>&lt;15 kg</td>
<td>30mg</td>
<td>twice daily</td>
</tr>
<tr>
<td>15-23 kg</td>
<td>45mg</td>
<td>twice daily</td>
</tr>
<tr>
<td>23-40 kg</td>
<td>60mg</td>
<td>twice daily</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>75mg</td>
<td>twice daily</td>
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All are given for 5 days for early mild cases, for severe cases however higher doses may be needed. This represents a dose of ~2mg/kg/dose, which is as twice the strength of the adult dose, and had been established by pharmacokinetic studies done in this age group.

The US FDA had asked the Drug sponsor “Roche Pharmaceuticals” to collect pharmacokinetic and safety data from children as young as less than one month of age. Subsequent data collected during juvenile animal toxicity studies indicated there is a potential risk of central nervous system (CNS) toxicity in younger infants. Realizing the difficulty to monitor CNS toxicity in infants less than one year of age, The Division of Antiviral Drug Products (DAVDP) thus, removed the request for studies in neonates and infants less than one year of age.[1, 2]

What measures can protect this age group?

Basic infection control precautions such as; keeping the child away from sick people, frequent hand-washing and flu shots (for children over 6 months old and caregivers) may be the best way to prevent the disease in this age group.[3]

References:

3. Canadian Adverse Reaction Newsletter (JAMC • 3, FÉVR. 2004; 170 (3).
The first reported Myopathy and rhabdomyolysis with Fluvastatin-Gemfibrozil

Statins and fibric acid derivatives have complementary effects on mixed hyperlipidemia. However, such combination therapy increases the risk of myopathy (destruction of muscle cells that is characterized by increase in the level of creatinine kinase up to 10 times the upper limit, and accompanied with muscle pain and weakness) which may result in life-threatening rhabdomyolysis (release of myoglobin from the destructed muscle cells that would accumulate in and compromise the kidney function).

Several early reports have suggested that combination fluvastatin–gemfibrozil therapy is both effective and safe in mixed lipid disorders.[1-4] However Akoglu H, et al had recently reported a case of acute hepatic injury and acute renal failure secondary to rhabdomyolysis associated with fluvastatin–gemfibrozil combination therapy for hyperlipidemia.[5]

A 56-year-old woman with a history of hyperlipidemia presented with fatigue, weakness in her lower extremities, and red-colored urine that happened one month after she had started combination therapy of fluvastatin 80 mg/day and gemfibrozil 1200 mg/day. The patient had a serious loss of motor function in the upper and lower extremities. Her laboratory tests revealed severe liver enzyme elevation and abnormal renal function. Abdominal ultrasound did not show hepatic cholestasis, renal parenchymal abnormality, or obstruction.

This report should draw the clinicians attention toward careful consideration of the risks and benefits of treating dyslipidemia with fluvastatin–gemfibrozil combination therapy.

References:

1. Spence JD, Munoz CE, Hendricks L, Latchinian L, Khouri HE. Pharmacokinetics of the combination of fluvastatin and gemfibrozil. Am J Cardiol 1995;76 suppl 1:80A-3A.
2. Smit JW, Jansen GH, de Bruin TW, Erkelens DW. Treatment of combined hyperlipidemia with fluvastatin and gemfibrozil, alone or in combination, does not induce muscle damage. Am J Cardiol 1995;76(suppl 1):126A-8A.