| **Brief Introduction** (max 300 words) | Coronary artery disease is the major cause of death in the developed societies and an emerging health problem in the developing countries. Ischemic heart disease cause millions of deaths worldwide and remains the leading cause morbidity and mortality in the developed world.1 Myocardial ischemia (also known as angina) refers to chest pain or discomfort that occurs when the heart muscle is not getting enough oxygen-rich blood for a short period of time. The inadequate blood flow is caused by narrowed coronary arteries (atherosclerosis of the coronary arteries), which are the vessels that supply blood to the heart.2 Oxidative stress is one of the most important pathogenic elements of atherosclerosis development. In fact, it accompanies the atherogenic process at all stages of its development, from those related to endothelial dysfunction to the formation of fibroproliferative lesions.3 It may also contribute significantly to destabilisation of artery wall plaques. As a result of oxidative stress in the vascular wall, oxygenated forms of LDL (Ox-LDL) are formed and they are taken up by macrophages contributing to the formation of foam cells which are the basis for the development of early atherosclerotic lesions.4 Ox-LDL also stimulate the macrophages to increase the production of pro-inflammatory cytokines including IL-6 which in turn stimulates the synthesis of acute phase protein, (CRP), in the liver.5 The statins are the most potent lipid-lowering agents currently available, and the newer agents have been shown to reduce LDL levels. Statins lower LDL primarily through the inhibition of the HMG-CoA-reductase enzyme, which catalyzes the first committed step of cholesterol synthesis in the mevalonate pathway. Statins also decrease triglyceride levels to a lesser degree, presumably through the inhibition of its synthesis in the liver and enhancement of lipoprotein lipase enzyme activity in the adipocytes.6,7 There is a study has shown that in patients with CAD treated with statins, the reduction in the incidence of re-infarction or cardiovascular mortality is not only related to LDL-cholesterol lowering effect but also to decreasing of CRP level below 2 mg/l |
which is only possible with rather high doses of statins that limits their availability in common use.8,9

CRP appears to be correlated to heart disease risk. Inflammation (swelling) of the arteries has been linked to an increased risk of heart disease, heart attack, stroke, and peripheral arterial disease. It seems, however, that the use of moderate doses of statins in combination with natural multifunctional antioxidants, could represent an alternative therapeutic approach.10

Over the past several years, great achievement has been made in the treatment of cardiovascular disease, which have depend on the use of experimental animal models. With the use of disease models in preclinical research, a large amount of information has been generated, which has outlined the pathogenesis, progression and mechanisms underlying cardiovascular disease at the cellular and molecular level. This has allowed the development of many effective treatment strategies.11

Epidemiological studies clearly show that the diet plays an important role in preventing degenerative diseases such as coronary heart disease (CHD), the leading causes of mortality and morbidity.12 Wheat germ (WGO) is a concentrated source of nutrients, especially Vitamins E and B complex, minerals including iron and calcium, as well as some protein. WGO is an important source of n-3 fatty acids, which may exert antiatherosclerotic effect.13

WGO is one of the richest sources of natural vitamin E. It is believed that out of all the antioxidants, vitamin E may offer the greatest protection against heart disease. One physiological role of vitamin E is its ability to react with and quench free radicals in cell membranes and other lipid environments, thereby preventing polyunsaturated fatty acids (PUFA) from oxidation, and inhibiting oxidative modification of low density lipoprotein (LDL) cholesterol.14

Indeed, several large population studies have demonstrated that vitamin E levels may be more predictive of developing a heart attack or stroke than total cholesterol levels. In addition to offering protection against cardiovascular disease, WGO could play a major role in the actual treatment of heart disease and recovery from strokes.15

The effect of WGO on myocardial ischemia has not previously been investigated.
The aim of this study is to verify the hypothesis that a reduction in level of oxidative stress using wheat germ oil in experimental CVD model treated with statins may augment the statins’ reduction in cardiovascular risk markers.

1- To evaluate the possible antioxidant protective effects of WGO separately and in combination with statins in myocardial ischemia by measuring the oxidative stress marker MDA and the antioxidants GSH & vitamin E.

2- To evaluate the possible protective effects of WGO separately and in combination with statins in ameliorating lipid profile by measuring TG, total cholesterol, HDL, Ox-LDL and Apo A-I.

3- To estimate and compare the possible effects of WGO separately and in combination with statins on cardiac disease progression by measuring the cardiac markers CRP and CK.

Methodology (max 300 words)

Research Protocol:

The study will include 48 rats. They will be housed in healthy condition at temperature room before starting the experimental acclimatization. After acclimatization rats will be divided into four groups of 12 rats each.

Subjects:
The animals will include 48 rats that will be divided into 4 groups as followings:

1- 12 rats serve as control (normal rats) will be kept on normal standard diet (group I).

2- 12 rats will be treated with isoproterenol subcutaneously (85mg/kg) for 2 consecutive days for induction of myocardial ischemia (group II).

3- 12 rats will be treated prophylactic with statins only [rats will be subcutaneously injected with atorvastatin (10 mg/kg/ day) for three days] before induction of myocardial ischemia (group III).

4- 12 rats will be treated prophylactic with combination of statins [subcutaneous injection of atorvastatin (10 mg/kg/day) for 3 days] and wheat germ oil [rats will be fed on the diet supplemented with 10% of wheat germ oil for 3 weeks orally] before induction of myocardial ischemia (group IV).

At the end of the experimental period, then rats will be sacrificed. Blood samples will be collected from the aorta for serum separation. Serum samples will be frozen at -80°C until biochemical analysis.
Biochemical assay:
1- Measurement of TG, HDL, total cholesterol, Oxidized low density lipoprotein and Apo A-I:
   a- Triglyceride (TG), high density lipoprotein (HDL) and total cholesterol will be measured using a Reflotron plus Clinical Chemistry Analyser (Reflectance photometry measurement)
   b- Oxidized low density lipoprotein (Ox- LDL) & apo lipoprotein A-I(Apo A-I) will be measured using appropriate ELISA kits following the manufacturer instruction.

2- Measurement of cardiac markers:
   a- CRP will be measured using an appropriate ELISA kit following the manufacturer instruction.
   b- CK will be measured using a Reflotron plus Clinical Chemistry Analyser (Reflectance photometry measurement)

3- Measurement of oxidative markers and antioxidants:
   a- Measurement of reduced GSH will be measured using colorimetric assay kit based on the glutathione recycling system by 5, 5'-Dithio-bis (2-nitrobenzoic acid) (DTNB).
   b- Malondialdehyde (MDH) will be also measured using colorimetric assay kit based on the Schiff reagent by thiobarbituric Acid (TBA).

4- Measurement of vitamin E:
   Vitamin E will be measured using high performance liquid Chromatography (HPLC)

<table>
<thead>
<tr>
<th>The project is applicable within (months)</th>
<th>12</th>
</tr>
</thead>
</table>

References (max 300 words)


3- Steinberg D. Low density lipoprotein oxidation and its


<table>
<thead>
<tr>
<th>Number</th>
<th>Reference</th>
</tr>
</thead>
</table>

