Clopidogrel is an oral thienopyridine anti-platelet drug which selectively inhibits the adenosine diphosphate mediated platelet aggregation. It is worldwide used for the long term prevention of atherothrombotic events, including, myocardial infarction, stroke, peripheral arterial disease, acute coronary syndrome and cardiovascular death in patients at risk of such outcome. The innovator drug product containing Clopidogrel hydrogensulfate is produced and marketed by Sanofi-Aventis and Bristol-Myers Squibb under the brand name of Plavix®. The original patent expiration date of Plavix® was in 2008, except in the United States it was extended until November 2011. In countries where Plavix® has lost patent protection and in others where patents are not in force, generic versions were legally introduced and sold at more affordable prices. According to the FDA, generic drugs are therapeutically equivalents to their brand name counterparts. They are bioequivalent, and pharmaceutically equivalent with respect to the active ingredient, strength, dosage form, route of administration and intended use. For most drugs, bioequivalence testing should enable clinicians to substitute generic for innovator products. However, generic drugs may differ by the amount or type of the excipients, source of the raw materials and the manufacturing process. Thus, generic substitution may affect both the bioavailability and the tolerability of the drug and may result in reduced patient adherence to treatment. The aim of this study was to compare seven generic formulations of Clopidogrel available in the Lebanese market and some Arab countries (Egypt and Syria) to the innovator drug product Plavix®(Clopidogrel hydrogensulfate equivalent to 75mg Clopidogrel base) for its physical appearance, dimensions, hardness, mass uniformity, disintegration time, content uniformity, dissolution 88 rate, assay and optical activity in order to determine whether one or more of these generics can substitute Plavix®, providing a cost-saving and cost-effective alternative for cardiac patients. Differences were found between the innovator drug and some of the generics related to the physical appearance, disintegration time, hardness, and the specific rotation which were significant for most of the tests. Although the observed differences, the innovator drug and the seven generics met the USP 2007 specifications for content uniformity, weight uniformity, assay and dissolution rate tests. Accordingly, they can be prescribed as per the stated
pharmacological indication as a cost saving alternative to Plavix®. However, the dissolution rate profiles of the tested generics were significantly different than that of Plavix®. This may lead to significant changes in the bioavailability of the drug and consequently may affect homeostasis. But since Clopidogrel is a Biopharmaceutics Classification System (BCS) class II drug, these findings should be confirmed using appropriate dissolution media that simulate the in vivo performance in order to achieve adequate In vitro-In vivo correlation or biowaiver. In conclusion, health care professionals can prescribe either the innovator drug or one of the tested Clopidogrel generics as cost saving alternatives. But, it is not recommended for prescribers to change the prescribed brand during the course of treatment to avoid changes in the bioavailability of such a potent drug. In addition, studies relating clinical safety and efficacy to the optical rotation of Clopidogrel need further investigation.