Chapter 13
FLEXIQULE™ SAFETY STUDY: NON-INTERFERENCE WITH ANTICOAGULANTS & ANTIPLATELET AGENTS

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Antiplatelet agents and anticoagulants are increasingly used in the prevention of cardiovascular and thrombotic events. This pilot study evaluates the effect of a new anti-inflammatory agent (based on Boswellia) on the antiplatelet action and anticoagulant activity in subject using FlexiQule™ for at least a week for the management of knee arthrosis.

The in vivo bleeding time is performed with 2 horizontal skin cuts; excess blood is removed using a filter paper and the time is recorded until bleeding stops (exactly as described by Harrison P. Platelet function analysis. Blood Reviews (2005) 19, 111–23).

The *bleeding time (BT)*, developed by Duke, was the first in vivo test of platelet function and was still regarded as the most useful test of platelet function until the early 1990s.
The bleeding time is the time taken for bleeding to stop after an incision is made into the skin, usually into the anterior surface of forearm. The test has been refined and standardized with the use of a sphygmomanometer cuff, room temperature control and a spring-loaded template device to make standard sized cuts within the skin.
Normal BT are usually between 2 and 10 min, whereas severe platelet defects can result in a BT >30 min. Despite its apparent simplicity, the test needs attention to be reproducible. BT does correlate well with the bleeding tendency within individual patients; it is widely – but possibly wrongly – considered that an accurate bleeding history is a more valuable screening test for bleeding (but not definitely for thrombosis).
Recent data suggests that the BT is not predictive of either myocardial infarction (MI) or ischemic stroke. The clear ad-

vantage of the BT is that it does study natural hemostasis and the role played by the vessel wall in this process. The test does not require expensive equipment or a laboratory and is not prone to laboratory variables associated with blood sampling and anticoagulation.
In this pilot experience (to establish a study model) BT was eveluated in 12 subjects (age 64.3;4.5 all males) using FlexiQule™; no other treatments or clinical conditions was used. Before FlexiQule™ supplementation BT was on average 4.33;1.1 (range 3.3-6.3) min. After 2 weeks of FlexiQule™ supplementation (for knee arthrosis) the average BT value was 4.26;1.3 (range 3.2-6.1) min.
Aspirin (Cardioaspirin 100 mg/day) had been used in the two weeks of FlexiQule™ management (these patients had been in chronic antiplatelet management for at least 6 months and had no tolerability problems).
Comparable results were obtained with Plavix (8 patients) and ticlopidine (6 patients) used at standard dosages with a maximum variation of less that 2.5% of the BT (less than the variability value for the test).

Anticoagulation was also evaluated in 7 patients using Coumadin.
Before the two weeks with FlexiQule™ their international normalized ratio (INR) was on average 2.97;0.23; after 2 weeks with FlexiQule™ the INR it was basically unchanged (2.98;0.2).
New anticoagulants, now in the market, are expanding their applications.
Therefore, present studies. now in progress are also looking at these new products.

In conclusion, FlexiQule™ – even in a limited study – do not change the antiplatelet action of the most common antiplatelet agents and do not seem to alter, in stable patients the value of anticoagulant treatment after two weeks of supplementation.

References

1. Rodgers RP, Levin J. A critical reappraisal of the bleeding time. Semin Thromb Hemost 1990;16:1–20.
2. Elwood PC, Pickering J, Yarnell J, et al. Bleeding time, stroke and myocardial infarction: the CARE Philly prospective study. Platelets 2003;14:139–41.