

CONCLUSIONS

This doctoral thesis was focused onto the synthesis of new quaternary ammonium salts of triterpenoids from lupane, oleanane and ursane family for *in vitro* assessment of following biological activities: anti-HIV, antimicrobial, antiinflammatory and cytotoxic. Results are summed up in following points:

1. Author co-operated pilot project of industrial isolation of betulin (**1a**) from approximately 400 kg of birch bark. Furthermore, research of side products and optimisation of preparation of bromoethyl-esters triterpenic acids was concluded.
2. Precursors for preparation of quaternary ammonium esters, bromoethyl-esters **2a**, **3f**, **3i**, **11b**, **12b**, **14a**, **15a**, and chloroethyl-ester **3g**, were synthesised.
3. Six series of compounds, each consisting of three quaternary salts and one tertiary amine, were synthesised from betulinic acid (**1b**), oleanolic acid (**1c**), ursolic acid (**1c**), oxoacid **3e**, platanic acid (**11a**) a dihydrobetulinic acid (**12a**). Experimental procedures are suitable for bulk syntheses. Other quaternary salts of triterpenoids were also prepared.
4. Oxoacid **3e** was derivatised to yield group of heterocyclic hydrochlorides **6a**, **6b**, **6d**, **6f** and group of heterocyclic salts **6c**, **6e**, **6g**.
5. All new compounds were assessed *in vitro* for cytotoxic activity against T-lymphoblastic leukemia CEM in research facility of doc. MuDr. Marián Hajdúch, PhD in LEM, FN Olomouc. 9 derivatives shown high cytotoxic activity with $IC_{50} < 10 \mu\text{mol/l}$ (**3i**, **8b**, **10f**, **11e**, **11g**, **12d**, **12e**, **12f**, **15c**). Perspective are mainly derivatives of ursolic acid (**1c**). 8 derivatives (**4e**, **10f**, **11e**, **11i**, **12d**, **12f**, **14c**, **14d**) was also picked for screening against panel of 10 tumor cell lines. It was concluded that cytotoxic activity is sustained against all the lines including resistant and with changed phenotype.
6. Selected compounds, were assessed for antimicrobial activity by research group of doc. RNDr. Jan Hlaváč, CsC. UP Olomouc. Antimicrobial activity was observed on 4 compounds **4a**, **14b**, **14c**, **14d**.

7. As a part of this thesis 40 new compounds were prepared and characterised: **2b, 3g, 3i, 3a, 3b, 3c, 3d, 3e, 6a, 6b, 6c, 6d, 6e, 6f, 6g, 7a, 8b, 9c, 9d, 10f, 11b, 11c, 11d, 11e, 11f, 11g, 11h, 11i, 11j, 12c, 12d, 12e, 12f, 14c, 14d, 14e, 15a, 15c, 15d, 15e.**
8. Results were covered by Czech patent and are licensable to the industrial partners.