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1 **Evaluation and Analysis of Environmentally Sustainable**
2 **Methodologies for Extraction of Betulin from Birch Bark with Focus**
3 **on Industrial Feasibility**

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18

19 **Abstract**

20 Betulin from birch bark was extracted using two principally different extraction methodologies -
21 classical Reflux Boiling (RB) and Pressurized Liquid Extraction (PLE). The extraction methods
22 were analyzed both based on recovery and purity as well as for RB industrial feasibility. The
23 purity and recovery for the different extraction methods were analyzed using High Performance
24 Liquid Chromatography (HPLC) coupled with three different detection principles; Diode Array
25 Detector (DAD), Mass Spectrometry (MS) and Charged Aerosol Detector (CAD). The
26 chromatographic purity was determined by all detectors whereas the DAD was used also for
27 complementary gravimetric calculations of the purity of the extracts. The MS detections (in MS
28 and MS/MS modes) were mainly used to characterize the impurities. Two steps to increase the
29 purity of RB extracts were evaluated – pre-boiling the bark in water and precipitation by adding
30 water to the extract. Finally, the methods were compared in terms of amounts of betulin produced
31 and solvent consumed. The RB method including a precipitation step produced the highest purity
32 of betulin. However, results indicate that PLE using three cycles with the precipitation step give
33 similar purities as for RB. The PLE method produced up to 1.6 times higher amounts extracted
34 compared to the RB method. However, the solvent consumption (liter solvent/gram product) for
35 PLE was around 4.5 times higher as compared to the classical RB. PLE performed with only one
36 extraction cycle gave results more similar to RB with 1.2 times higher yield and 1.4 times higher
37 solvent consumption. The RB process was investigated in industrial scale using a model approach
38 and several important key-factors could be identified. The most energy demanding step was the
39 recycling of extraction solvent which motivates that solvent consumption should be kept low and
40 calculations show a great putative energy reduction by decreasing the ethanol concentration used
41 in the RB process to lower than 90%.

43 Introduction

44 A vast amount of birch bark is obtained annually as a by-product from the forest industry; a
45 recent estimate for only Sweden - the world's second largest producer of processed forest
46 products - is 1-2 million m³/year.¹ The white outer bark contains high amounts of betulin (up to
47 30% of dry weight)^{2, 3} together with low amounts of betulinic acid⁴ which could be used for other
48 purposes than energy production which is currently the most common use.⁵ Betulin is widely
49 used in cosmetics⁶ and is also a precursor for synthesis of betulinic acid⁷ which has important
50 medical properties, such as antitumor^{8, 9}, anti-inflammatory^{10, 11} and anti-HIV activities.^{12, 13}
51 Therefore, a cost-effective purification process for these compounds with low environmental
52 impact is highly desirable. Life cycle assessment has been used to compare two methods for
53 extraction of betulin from birch bark – leaching into ethanol at ambient temperature and
54 extraction using liquid carbon dioxide (50 bar, 16°C) with 20 w% ethanol as a co-solvent.¹ The
55 latter was concluded having lower environmental impact. However, betulin was not purified in
56 the extraction but rather just determined in terms of concentration in the ethanol extract.

57 There are numerous studies exploring different extraction techniques for betulin in birch bark,
58 including pressurized liquid extraction (PLE),¹⁴ supercritical fluid extraction (SFE),¹⁵ microwave
59 assisted extraction (MAE),¹⁶ and classical reflux boiling (RB) or leaching.¹⁷ While PLE and
60 MAE require special equipment, the increased temperature and pressure usually utilized is
61 believed to allow for more exhaustive extraction of the target compounds as compared to
62 classical RB. On the contrary, SFE is known as a more selective extraction technique.¹⁸ None of
63 the published studies calculated the energy usage necessary to compare different methodologies
64 in terms of betulin production. Furthermore, only a few studies actually did purify betulin from
65 the extract, and if they did, the method for determination of the purity varied largely, resulting in

66 non-comparable or even erroneous results. For more information about the chemistry and general
67 processing of birch bark, the reader is referred to the comprehensive review by P. Krasutsky.¹⁹

68 The required purity of the extracted target compound depends on the intended use of the final
69 product. Plant extracts intended for use in medical products are regulated e.g. by the Food and
70 Drug Administration in the USA and European Medicines Agency in the EU.^{20,21} Should the
71 same extract be used as a chemical of technical quality, it does not have the same stringent
72 requirements. In fact, “technical quality” does not seem to be a well-defined term; descriptions
73 like “reasonable quality”²² and “do not have an established standard set for quality and impurity
74 levels”²³ are used by some major suppliers.

75 The aim of this study is to find a suitable strategy for producing betulin with an appropriate purity
76 and quality while considering environmental aspects such as solvent and energy consumption.
77 This involves first a careful analytical evaluation of promising and environmentally sustainable
78 extraction principles (RB and PLE). Secondly, utilizing different detection principles such as
79 mass spectrometry (MS), UV/vis spectroscopy (using a diode array detector, DAD) and charged
80 aerosol detector (CAD) coupled with HPLC to determine the purity and recovery of the
81 extraction methods. Finally, the industrial feasibility of the most promising extraction technique
82 is investigated in more detail by establishing mass and energy balances for industrial scale
83 extraction, and solvent recovery processes based on reliable experimental data. Additionally, SFE
84 was tested as a potential extraction method but was not pursued further due to poor performance,
85 see Supplementary information.

86 **Results and Discussion**

87 In this study, a number of screening experiments were performed for extraction of betulin from
88 birch bark utilizing RB and PLE and the results were evaluated based on recovery, purity and
89 solvent consumption. Supercritical Fluid extraction (SFE) was also tested but was dropped due to
90 high solvent consumption, low recovery and no additional purity compared to PLE and RB, see
91 Supplementary information. The most promising extraction method for scale-up was thereafter
92 investigated in terms of industrial feasibility and environmental sustainability, taking mass and
93 energy balances into account. In Figure 1, the birch wood process is presented. The part of the
94 process investigated in this study is marked with dashed lines.

95 **Determination of suitable conditions for extraction by reflux boiling**

96 Several things were explored prior to the more in depth analytical investigations. First, two
97 different solvents were considered for the RB experiments; ethanol and acetone. Acetone was
98 rejected because it did not provide any apparent advantages regarding yield and purity compared
99 to the more environmentally sustainable ethanol, see Table 1. Secondly, the suitable boiling time
100 in the RB was evaluated based on purity and extracted amount of betulin, see Table 1. 10 min
101 boiling time was selected because only a minor increase in yield was observed for longer boiling
102 times. Finally, ethanol RB with or without pre-boiling of bark in water to remove potential
103 hydrophilic contaminations was evaluated. In Figure 2, chromatograms from RB extracts purified
104 by different means are presented. As can be seen, some impurities are removed with the pre-
105 boiling step; 9 out of 42 peaks are removed and more still have been reduced to some extent
106 (DAD data). However, the later precipitation step in the process is much more efficient in
107 removing impurities; 26 out of 42 peaks are completely removed and the remaining peaks have
108 been greatly reduced. Thus pre-boiling in water would not substantially increase the purity of the

109 target compound further in this particular case (see Supplementary information Table S1, Table
110 S2 and Table S3 for more information).

111 **Determining purities and extraction efficiencies of the methods**

112 Determination of purity is not trivial. For example, for UV-measurements it is required that the
113 compounds have chromophoric groups whereas in MS the compound need to be chargeable or be
114 charged to give signal and for CAD the compound volatility should not be too high (must have
115 lower volatility than the mobile phase). In addition, standard compounds are needed for both
116 analytes and all the impurities. One possible exception is if CAD is used since this detector is
117 considered being more generic, at least for non-volatile compounds. The purities using DAD,
118 CAD, MS and gravimetric as well as the extraction efficiencies and solvent consumption are
119 summarized in Table 2. The principal different methods for estimating the purity gave different
120 results and in general, the more unselective detector CAD gave the highest purity, as discussed
121 further below. The main aim with MS detection was not to evaluate the purity but instead to
122 characterize the impurities in a more qualitative way and see how these patterns changes for
123 different extraction methods and operational settings.

124 In the Supplementary information we have detailed the data even more: the total ion
125 chromatograms (TIC's) and extracted ion chromatograms (XIC's), can be found in Figure S1
126 with peak data in Table S3 (RB extracts), Figure S2 with peak data in Table S4 (PLE) and Figure
127 S3 with peak data in Table S5 (SFE). Triterpenes previously reported in birch bark are for
128 example betulonic aldehyde, betulone, betulonic acid, betulonic aldehyde and lupeol and β -
129 amyryrin.^{3, 19} Among the impurities are compounds showing similar fragmentation pattern as
130 betulin, betulonic acid and the triterpenes mentioned.²⁴ For example peak 17 is assigned as
131 betulonic acid, however the substituent (230 Da, at m/z 685) was only observed in one replicate.

132 Furthermore, two peaks show signals matching betulin with substituents; peaks 14 (betulin with a
133 26 Da substituent, m/z 469) and 19 (betulin with a 75 Da substituent, m/z 518). Peak 19 also
134 shows a signal which probably is a water adduct (m/z 461) or from the loss of parts of the
135 substituent mentioned above. Detailed MS and MS/MS data of betulin, betulinic acid and some
136 of the major impurities along with possible identities are shown in Supplementary information,
137 Table S6.

138 Purities determined by gravimetric analysis (see procedure in Supplementary information) gave
139 lower values than those obtained both by DAD and CAD, indicating that there could be several
140 impurities not detected by the detectors, see Table 2. Many times this is observed because the
141 contaminations are unsuitable for one or more of the detectors, such as lack of a chromophore for
142 DAD or poor ionization for MS, or because they occur at levels too low to give a response which
143 would be integrated (see Supplementary information). Table 2 shows that the precipitation step
144 results in the highest purity, both for RB and PLE. In order to investigate where the observed
145 extra contaminations in the gravimetric analysis originate from, the precipitate from the RB was
146 dissolved in ethanol, filtrated and precipitated again. The analysis of this sample showed to have
147 similar purity both for gravimetric and DAD. This clearly indicates that insoluble material, which
148 was also observed in the filter (probably dust and cellulose), are present in the first precipitate.
149 Because CAD, DAD and MS methods are based on chromatographic separations these
150 contaminations are lost in the sample preparations filtration steps, and as a consequence the
151 estimated purity is overestimated. To improve the process, finer filters after the leaching step was
152 used (102 Double Ring filter paper). The gravimetric purity with the additional filtration step
153 without water pre-boiling was determined to 60.2 % and 63.1% after the precipitation step. These
154 gravimetric purities are similar to the ones observed with birch bark pre-boiled in water after the

155 precipitation step, see Table 2. Fourier transform infrared spectroscopy (FTIR) analysis showed
156 that the library hit against wood decreases and hit against betulin increases with process steps and
157 filtration followed by precipitation had the same quality using birch bark with or without pre-
158 boiling step. In the Figure S4 photos of dried betulin process fluids or precipitates are presented
159 for morphological comparison.

160 When the RB extracts purified by precipitation are compared before and after the precipitation
161 step the gravimetric purity is significantly increased while only a slight (not statistically
162 significant) decrease in extracted amount occurs, based on analysis of variance (ANOVA) (data
163 not shown). This indicates that the purification should be performed on the other extracts as well.
164 ANOVA (data not shown) also suggests that adding also the pre-boiling step affects neither the
165 extracted amount nor the final purity to a notable extent (comparing extracts purified only by
166 precipitation to extracts purified by both pre-boiling and precipitation). As a consequence we
167 draw the conclusion that the pre-boiling step could be omitted from the final process without a
168 reduction in purity, assuming precipitation is performed.

169 The greatest extracted amount was obtained by PLE using three cycles; reaching a total of 79
170 mg/g bark, see Table 2. However, the amount of betulin produced is approximately 1.6 times
171 more than RB but with a solvent consumption (liter solvent per gram product) of 4.5 times
172 higher. The value obtained for each cycle could be of interest if a thorough analysis of the
173 economic feasibility for scaling up should be investigated, as it would then be possible to
174 determine if only one or two cycles should be used which would reduce solvent consumption. For
175 instance, using only one extraction cycle in PLE and introducing a precipitation step resulted in
176 pure product (Figure S5) with 1.2 times higher yield and 1.4 times higher solvent consumption
177 compared to RB. However, RB still outperforms PLE in terms of purity of the product, see Table

178 2. Both additional steps in RB (pre-boiling and precipitation) result in increased purity, with the
179 exception for MS detection (which was mainly used for characterization of impurities as
180 discussed above). None of these additional steps result in a significant loss of betulin so
181 combining this with the data in Supplementary information Table S7, showing that many
182 impurities are extracted by all three techniques, the potential of increasing the purity of PLE
183 extract is apparent as can be seen in Supplementary information Figure S5.

184 **Industry feasibility of the RB extraction process**

185 The RB extraction process using ethanol was selected for the further modelling of industrial
186 implementation as it performed well in terms of yield and purity and also because the process
187 utilizes both low temperature (*ca.* 78°C) and pressure (ambient). The mass and energy balances
188 for RB extraction was established based on experimental data and the process configuration and
189 production data from Gruvöns Mill, Sweden. The process sequences used in the laboratory
190 extraction tests were modelled and applied to the total birch bark flow from the debarking
191 process. After initial rough energy calculations, two additional unit operations were added to the
192 simulation model compared to the laboratory tests in order to lend the simulated case more
193 industrial relevance: (A) ethanol distillation enabling ethanol recirculation and therefore reducing
194 the ethanol consumption by more than 40 tons/h and (B) ethanol evaporation from the bark prior
195 to bark combustion, saving more than 10 tons/h ethanol. Furthermore, the later adjustment is
196 necessary as the ethanol-saturated bark would otherwise generate approximately 100 MW heat in
197 the bark boiler, which would overload the bark boiler and impede combustion of Softwood bark
198 and other solid fuels generated on the site. The resulting model is shown in Figure 3. For
199 simulation, actual mill data and assumed parameters were used (*cf.* Table 3). The Wilson

200 thermodynamic model was used as it gives good correlation with actual vapor-liquid equilibrium
201 data for ethanol/water.²⁵

202 The main results from the Chemcad simulations are shown in Table 3. As can be seen, adding the
203 betulin extraction process to the mill entails significant new mass and energy streams. With the
204 simulated process configuration, the total mill low-pressure steam demand increases with 93
205 tons/h, corresponding to 56 MW of additional heat usage. The combustion of the dried birch bark
206 in the biomass boiler instead of the present wet bark only generates 4.5 tons/h additional steam.
207 In order to generate the remaining 89 tons/h steam, the biomass consumption is increased by 9.0
208 kg/s. The additional steam usage results in an additional power production of approximately 13.3
209 MW.

210 From an industrialization perspective, the large-scale betulin production outlined in this study
211 could be considered viable from a mass handling perspective. However, for the actual mill the
212 concept would be troublesome due to the high energy consumption, especially for ethanol
213 recovery. An additional steam production of almost 90 tons/h cannot be provided without very
214 significant investments in new boiler capacity. In order to identify a more feasible process
215 concept the main heat consumer, the distillation reboiler, should be addressed. When, for
216 example, the ethanol concentration from the distillation column increases from 90 to 95%-wt, the
217 energy requirements increases from approx. 30 MW to 100MW.

218 As shown above the major cost in the process is the recycling of ethanol. Extraction with lower
219 ethanol concentration than close to the azeotropic ethanol water mixture (95 vol %), used in this
220 study would be clearly beneficial from an energy consumption point of view and should be tested
221 in future work. Furthermore, a modified process configuration utilizing evaporation of the extract

222 prior to the precipitation might be a feasible method to reduce the distillation load and should be
223 verified in further laboratory trials. Finally, the potential for heat integration between streams
224 within such a modified betulin process as well as the mill's secondary heat streams should be
225 further investigated.

226 **Experimental**

227 **Chemicals**

228 For all extractions methods, 95% ethanol (Solveco, Rosersberg, Sweden) was used whereas the
229 RB method also used MilliQ water from a MilliQ plus system (Millipore, Billerica,
230 Massachusetts, U.S.A.).

231 For the analysis methods LC-MS grade methanol respectively acetonitrile from Fisher Scientific
232 (Västra Frölunda, Sweden) and water from Sigma Aldrich Chemie GmbH (Schnelldorf,
233 Germany) were used. Betulin, betulinic acid and progesterone (all $\geq 98\%$ purity) were obtained
234 from Sigma Aldrich Chemie GmbH and NaNO_3 ($\geq 99.5\%$ purity) from Merck (Darmstadt,
235 Germany).

236 **Standard preparation**

237 A stock solution of 0.540 mg/ml betulin was prepared in methanol and diluted to standards
238 ranging from 0.003 to 0.070 mg/ml. A standard reference sample was prepared containing 0.044
239 mg/ml betulin, 0.046 mg/ml betulinic acid and 0.032 mg/ml progesterone as Internal Standard
240 (IS).

241 **Sample preparation and handling**

242 Bark from birch (*Betula pendula*) was collected at Gruvöns Mill (BillerudKorsnäs, Grums,
243 Sweden) directly from the transport conveyor below the debarking machine. The collected bark
244 was dried at room temperature for a week and thereafter chopped twice in a garden compost
245 crusher. Finally, the processed bark pieces were frozen in a freezer at -18°C followed by a
246 “splash” of liquid nitrogen for making the bark brittle and thereafter directly processed in a food
247 processor to approximately 1 x 1 cm² pieces.

248 **Extraction by classical reflux boiling (RB)**

249 Three different types of experiments were performed to determine: (1) suitable boiling time
250 followed by two alternative ways to increase the purify the final product, either by (2) combining
251 RB with precipitation by adding water to the extract or (3) pre-boiling the bark in water prior to
252 extraction. All experiments were conducted at least in triplicates and stored in refrigerator (+8°C)
253 until analysis; all processed samples were analyzed the same day. For details see Supplementary
254 information.

255 **Pressurized liquid extraction (PLE)**

256 The PLE conditions were based on a previous study, in which a maximized betulin yield was the
257 aim.¹⁴ Extractions with 95% ethanol were performed using an ASE 200 (Thermo Fischer,
258 Germering, Germany) equipped with a solvent controller. The extraction was done in triplicate
259 and each extraction was performed in three cycles of 5 min each, with each cycle collected
260 separately. Internal standard was added to monitor solvent losses during storage. The samples
261 were stored at -18°C until analysis. The procedure is described in more detail in Supplementary
262 information.

263 Analysis

264 An Agilent 1100 series system (Agilent Technologies, Waldbronn Germany) with a Kromasil
265 C18 column (2.1 x 100 mm, with nominal particle size of 3.5 μm , AkzoNobel, Bohus, Sweden)
266 was used for separation of the extracts. The mobile phases consisted of LC-MS grade water (A)
267 and acetonitrile (B), and a linear gradient of 5-95% B over 30 min followed by 10 min at 95% B
268 was used. Three different detectors were used. A diode array detector (Agilent Technologies) was
269 used at 210 nm to evaluate betulin content and purity (210-400 nm was recorded). A Corona ultra
270 RS CAD (Dionex, Sunnyvale, CA) was also used for these purposes (gradient compensation was
271 utilized to keep the composition of mobile phase reaching the detector constant). A Q-Trap 3200
272 mass spectrometer (AB Sciex, Concord, ON, Canada) operating in positive ion mode with
273 atmospheric pressure chemical ionization (APCI) was used to collect MS and MS/MS data with
274 enhanced mass spectrometry (EMS) and enhanced product ion (EPI) experiments (100-1200 Th
275 was recorded in both experiments).

276 Determination of purity and amount extracted betulin

277 Chromatographic purity utilizing the DAD (210 nm) and CAD was determined by taking the area
278 ratio of the betulin peak to the total integrated area (excluding the contribution from IS if used)
279 between 3 and 44 min (area threshold: 5, height threshold: 1 for DAD and area threshold: 2,
280 height threshold: 0.3 for CAD). Since a gradient was employed for separation, blank subtraction
281 was performed for the DAD data. In addition gravimetric purity was determined from the
282 concentration obtained by DAD; the procedure is described in Supplementary information. From
283 the MS data, the total ion chromatogram was used to estimate the chromatographic purity and m/z
284 from MS (Extracted Ion Chromatograms, XIC's) and MS/MS were used to tentatively identify

285 potential impurities, though most impurities were of too low intensity to yield any MS/MS
286 signals.

287 **Calculations of mass and energy balances for industrial feasibility**

288 Mass and energy balances for RB extraction were calculated based on experimental data and
289 production data from Gruvöns Mill where the bark for the experiments were collected. Gruvöns
290 Mill is an integrated paper mill with an annual production of 685 kton/a based on softwood and
291 hardwood chemical pulping. Around 25 % of the used wood is birch. Debarking of birch wood
292 prior to pulping yields approximately 50 000 metric ton dry substance bark/year. The material
293 and heat balances process was modelled, using Chemcad 6.4.1, (Chemstations Europe GmbH,
294 Berlin, Germany).

295 **Conclusions**

296 In this study we have extracted betulin from birch bark utilizing two different methods: reflux
297 boiling (RB) and pressurized liquid extraction (PLE). The classical RB gave the highest purity of
298 betulin. Our results show that PLE did not give better selectivity towards the product than RB.
299 PLE with three cycles gave up to 1.6 higher amount extracted betulin as compared to RB. On the
300 other hand, the solvent consumption per gram product for PLE was around 4.5 times higher as
301 compared to RB. Using just the first cycle in the PLE process result in 1.4 times higher solvent
302 consumption and 1.2 higher amount extracted betulin compare to RB. Therefore, PLE is likely a
303 more energy-demanding and expensive process, since a larger amount of solvent is required in
304 the process and more advanced equipment is used. One could recycle the solvent to reduce the
305 cost, however, recycling ethanol is a quite energy-consuming process.²⁶ We also found that
306 pretreatment of birch bark with boiling water prior to the RB step to remove hydrophilic

307 contaminations did remove contaminations in the process fluid (*cf.* Figure 2); however, the
308 highest impact on purification of was accomplished by the introduction of a precipitation step.
309 The optimized RB process was selected as a model for industrial calculations for 50 000 ton of
310 birch bark. The RB method is suitable for scale-up and a number of potential process
311 modifications have been identified that would significantly improve the feasibility for large-scale
312 purification. Among others it could be demonstrated that ethanol concentration from the
313 distillation column < 90% results in drastically decreasing energy consumption. A further techno-
314 economical study is planned in which process parameters and heat integration will be optimized.
315 Extraction tests will be carried out in order to verify that betulin yield and purity can be
316 maintained. If successful, the proposed extraction and purification process can be used as a
317 valorization process in forest industry.

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367

368 **Figure captions**

369 **Figure 1.** A schematic overview how birch wood are processed and where our suggested extra
370 process steps fits into the whole process. The investigated part of the process is marked with
371 dashed lines.

372 **Figure 2.** a) Chromatograms recorded with DAD210nm after different means of purifying the
373 extract; no purification (upper black line, RB), pre-boiling in water (grey line, pre-RB) and
374 precipitation (lower black line, RB-pc). For increased clarity RB has been off-set by 20 mAU,

375 and pre-RB by 5 mAU. Betulin is labeled bet and betulinic acid ba. b) Magnification of part of
376 the chromatograms in a), with RB off-set by 5 mAU and pre-RB by 3 mAU. Peaks are labeled in
377 chronological order, according to the retention times in Supplementary information Table S7.

378 **Figure 3.** Process model for the leaching process.

Table 1. Reflux boiling as a function of boiling time. Chromatographic purities (DAD 210 nm) in percent of betulin peak area divided by the total integrated area and extracted amount betulin yield in mg/g dry bark for different boiling times and solvents. No blank subtraction has been made on these chromatograms.

Boiling time* (min)	Ethanol		Ethanol, pre-boiling		Acetone	
	% area	mg/g	% area	mg/g	% area	mg/g
0	37	39	48	41	45	40
5	42	53	61	48	53	39
10	49	59	60	53	46	43
15	44	49	61	47	47	43
20	47	64	62	61	52	48

*0 min is when the solvent started boiling, the extraction process had begun prior to this.

Table 2. Chromatographic purities of the extracts using different means, extracted amounts (mg betulin/g bark) and solvent consumption (l solvent / g betulin). Extracted amounts and solvent consumption were calculated based on DAD data. Reflux boiling extractions were performed as follows; (n): neither pre-boiling in water nor precipitation, (2): no pre-boiling in water but with precipitation, (3): pre-boiling in water but no precipitation and (b): both pre-boiling in water and precipitation. Results for PLE are presented as pooled extracts from three extraction cycles, first extraction cycle only (1st cycle), and for one PLE extract a precipitation step was included (p, 1st cycle). All values are given as average \pm standard error.

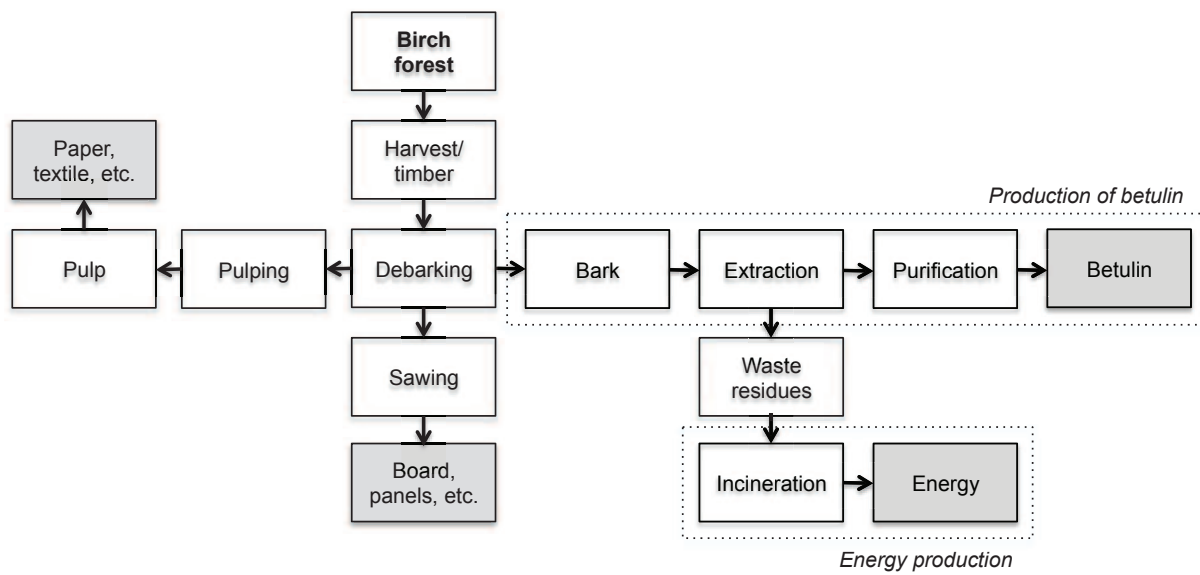
Extraction method	Chromatographic purity, DAD (%)	Chromatographic purity, CAD (%)	Chromatographic purity, TIC (%)	Gravimetric purity (%)	Extracted amount (mg betulin/g bark)	Solvent consumption (l solvent / g betulin)
Reflux boiling (n), ethanol	72.9 \pm 7.1	80.8 \pm 0.5	39.5 \pm 2.9	33.9 \pm 3.8	51.6 \pm 4.1	0.194 \pm 0.015
Reflux boiling (n), acetone	76.1 \pm 2.7	80.0 \pm 2.0	32.3 \pm 2.2	33.9 \pm 3.4	44.6 \pm 3.6	0.224 \pm 0.018
Reflux boiling (2), ethanol	85.3 \pm 3.6	87.1 \pm 0.4	28.6 \pm 3.6	60.9 \pm 1.7	47.5 \pm 7.5	0.210 \pm 0.033
Reflux boiling (2), acetone	86.5 \pm 2.6	86.5 \pm 3.5	36.2 \pm 1.6	59.3 \pm 4.3	44.5 \pm 1.7	0.225 \pm 0.009
Reflux boiling (3), ethanol	78.7 \pm 2.0	85.1 \pm 1.5	33.5 \pm 3.8	38.2 \pm 3.6	48.3 \pm 3.2	0.207 \pm 0.014
Reflux boiling (3), acetone	80.6 \pm 2.0	86.8 \pm 0.1	43.2 \pm 3.6	46.5 \pm 9.5	45.2 \pm 2.1	0.221 \pm 0.010
Reflux boiling (b), ethanol	87.6 \pm 2.8	86.4 \pm 0.1	30.8 \pm 4.4	62.8 \pm 8.6	48.6 \pm 9.4	0.206 \pm 0.040
Reflux boiling (b), acetone	85.6 \pm 3.8	90.0 \pm 0.7	39.6 \pm 2.2	60.1 \pm 1.8	45.1 \pm 2.3	0.222 \pm 0.011
PLE	72.6 \pm 4.0	77.9 \pm 1.7	34.8 \pm 7.2	17.0 \pm 3.1	76.7 \pm 8.1	0.980 \pm 0.106
PLE (1 st cycle)	73.3 \pm 8.0	82.0 \pm 1.5	57.5 \pm 7.3	25.4 \pm 4.0	62.5 \pm 9.8	0.254 \pm 0.040
PLE (p, 1 st cycle)	66.5 \pm 3.0	n.d.	n.d.	47.4 \pm 0.3	58.8 \pm 0.4	0.287 \pm 0.002

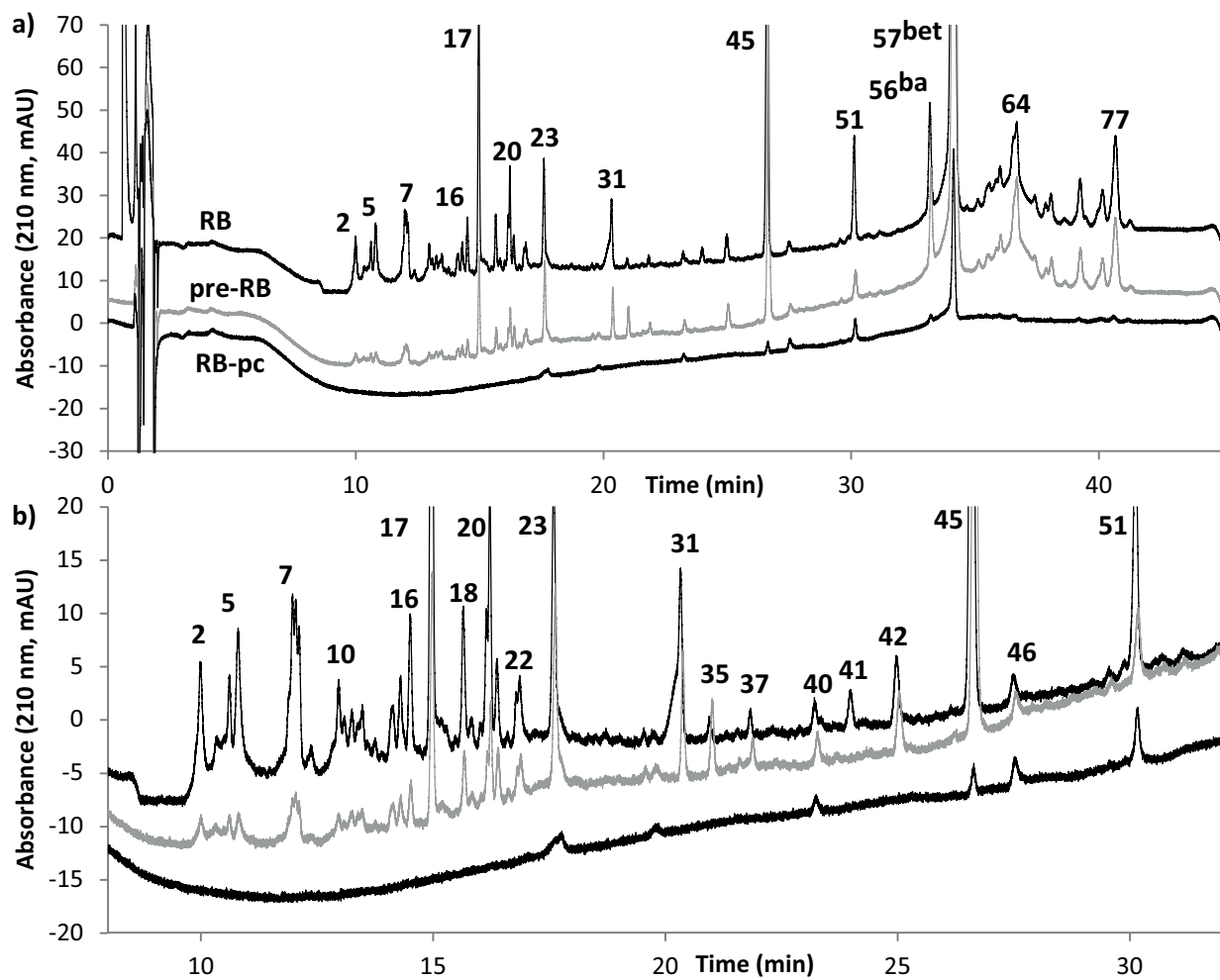
n.d. Not determined

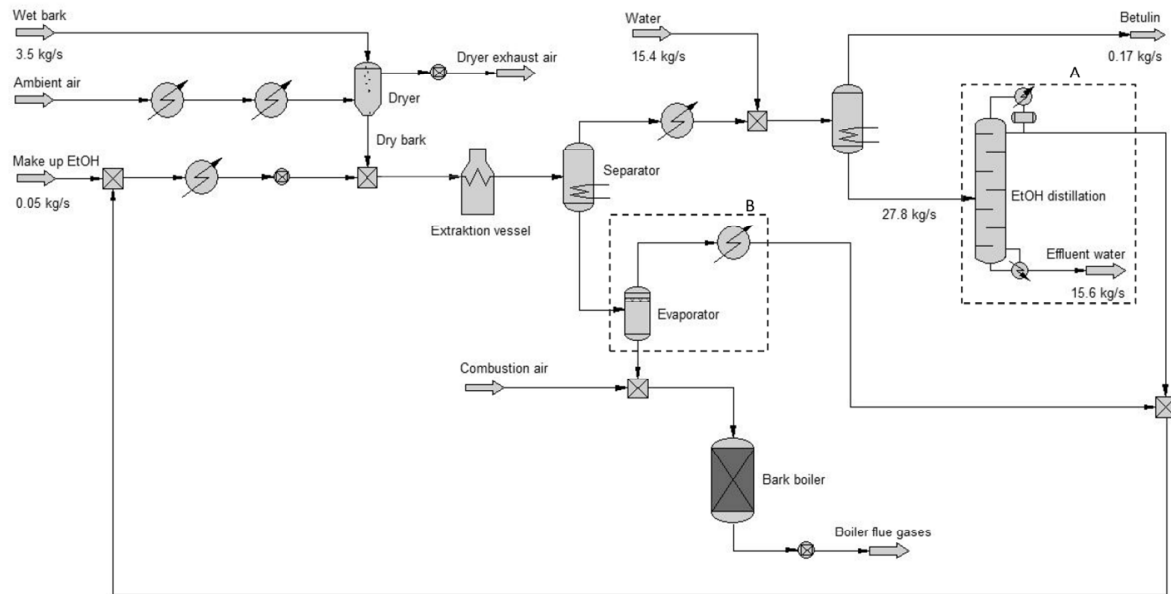
Table 3: Presentation of modelling assumptions and experimental data for the RB calculations.

The unit bar_a stands for the absolute pressure.

Modelling assumptions	
<i>Actual data from Gruvön Mill</i>	
Birch bark production, (tons/yr dry solids)	50 000
Bark dry content, (%)	50
Biomass boiler design capacity, (MW _{th})	90
Steam turbine	
Admission data, (bar _a /°C)	58/470
Low pressure steam (turbine outlet), (bar _a)	4.2
Biomass moisture content, (%)	50
<i>Assumed data</i>	
Biomass boiler flue gas temperature, (°C)	170
O ₂ in boiler flue gases (vol % wet)	6
Steam turbine	
Isentropic efficiency	0.80
Atmospheric distillation	
No of ideal stages	30
Feed stage	25
Bottom ethanol concentration, (% weight)	0.1
Calculated results	
Betulin production, (tons/yr)	2 500
Distillation reboiler duty, MW	49.4
Distillation condenser duty, MW	41.1
Change in mill power production, MW	13.3
Change in mill fuel consumption, (wet tons/a)	259 000







Evaluation and analysis of environmentally sustainable extraction of betulin from birch bark with focus on large-scale industrial feasibility



Evaluation and analysis of environmentally sustainable extraction of betulin from birch bark with focus on large-scale industrial feasibility
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