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Identification of Cost-Relevant Factors in the Production of a Triterpenoid Saponin in Hydroponically Grown Soapwort: A Case Study

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Abstract: The economically efficient, reproducible cultivation of plants containing valuable ingredients for pharmaceutical or cosmetic purposes is a challenge today. Although greenhouse cultivation is much more expensive than field cultivation, this may be justified by the high level of control over environmental conditions. However, a careful analysis of costs and the investigation of potential cost-reducing measures are essential. Here, soapwort (*Saponaria officinalis*) was grown in a greenhouse to identify factors influencing the production costs of the pharmaceutically relevant saponin SO1861 in the roots. The plants were grown hydroponically to facilitate harvesting. Three factors were identified as having a significant impact on production costs: the genotype of the plants, the method of propagation, and the type of lighting used in the greenhouse. Commercially available soapwort seeds do not have a defined genetic background. Cost simulations suggest that the cost of producing SO1861 can be significantly reduced by pre-testing plants for SO1861 production capacity, propagating plants from cuttings rather than seeds, and using light-emitting diodes instead of the more traditional high-pressure sodium lamps. The impact of these factors on the total production costs was calculated and discussed. A simplified version of the cost model, which can be used as a blueprint for estimating the costs of any other greenhouse crop, was also included in the supporting data.

Keywords: hydroponic cultivation; *Saponaria officinalis*; cost calculation; production costs; cost model; optimization

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1. Introduction

Plants are important sources of pharmaceutically active compounds [1]. As sustainability requirements make the collection of large quantities of plants from natural sources infeasible, the cultivation of plants that produce valuable chemicals is the way forward [2]. Greenhouse cultivation is promising for commercial use as it provides reliable harvests throughout the year and conditions can be easily adapted to the specific needs of the plants [3]. In addition, hydroponics can be used to facilitate root harvesting if the active ingredient is produced there [4].

Saponaria officinalis L., commonly known as soapwort, is a plant species that has been used for centuries for its medicinal and cosmetic properties [5]. Its roots contain triterpenoid saponins, which are natural surfactants that have applications in various industries, including the pharmaceutical, food, and personal care sectors [6]. With the growing demand for natural and sustainable ingredients, the cultivation of *S. officinalis* for the production of triterpenoid saponins has gained attention. For example, a group of these saponin compounds have been shown to have potent properties as agents for the transfection of mammalian cells. This process has been termed 'sapofection', while the saponin compound involved has been termed 'sapofectoside' and largely corresponds to the saponin SO1861 in the *S. officinalis* material [7]. SO1861 is a triterpenoid saponin consisting of an oleanane-type skeleton glycosylated in two places with in total nine sugar molecules [7]. To explore the potential of these potent compounds, larger amounts of sapofectosid need to be reliably produced. For this, greenhouse cultivation of soapwort plants is an interesting alternative to field cultivation. However, as such a contained cultivation is bound to be more expensive than growing plants outside, it is advisable to first determine the profitability and viability of the venture by estimating the manufacturing cost, also called cost of goods (CoG) [8]. The present CoG analysis involved evaluating the direct costs associated with growing, harvesting, and processing the soapwort plants as a basis for later purification of the sapofectoside SO1861. Factors such as labor, energy, and waste management are directly linked to the production of goods and determine the cost of producing one gram of SO1861. However, investment costs are typically not included in the CoG analysis because they are associated with the acquisition or upgrading of assets or infrastructure used in production, such as equipment, facilities, and technology [9]. These costs are not directly linked to the production of a specific unit of the product but are spread over the life of the asset or infrastructure. For the purposes of this study, investment costs such as the construction and maintenance of the greenhouse, cultivation unit, and metering equipment were not included in the calculations. CoG analysis can provide decision-makers with information on economic viability and the impact of cost-cutting measures and other business strategies.

This paper presents a simple model-based cost analysis of the production of SO1861 in the roots of soapwort in hydroponic greenhouse cultivation. Hydroponic systems have gained significant attention as a sustainable alternative to traditional soil-based agriculture, particularly in addressing challenges such as limited arable land, water scarcity, and soil degradation [10,11]. Recent advancements in hydroponic technologies, including nutrient management and environmental control, have demonstrated their potential to enhance resource efficiency and crop yields [11,12]. However, the economic feasibility of hydroponic cultivation for specialized compounds such as SO1861 remains underexplored, creating a critical gap in the literature. The aim of this study is to estimate the cost of production under different assumptions and to identify factors that are cost-effective for a crop focused on producing SO1861. The cost model includes various cost components such as labor, electricity, heating, water, materials, and waste, and considers the impact of different factors such as lighting, propagation, and plant genotype. We aim to provide insights into optimizing hydroponic systems for specialized crop production, thereby contributing to the broader understanding of hydroponic greenhouse cultivation. As these results are applicable to other hydroponic crops grown in greenhouses, a simple interactive table to estimate the costs directly attributable to cultivation has been included in the Supporting Data Section.

2. Materials and Methods

2.1. Plant Material and Growth Conditions

Seeds of *Saponaria officinalis* L. were obtained from two sources: gold nugget seeds, SG144 from Jelitto (Schwarmstedt, Germany), referred to as cultivar S3, and seeds 602850 from Vreeken's Zaden (Dordrecht, The Netherlands), referred to as cultivar S6. The seeds were pretreated by sterilization and incubation on wet filter paper at 20 °C for three days, followed by storage at 4 °C for 12 days. The seeds were then placed on rock wool plugs (Productno 51482; Grodan, Roermond, The Netherlands) in water in the greenhouse and germinated after three to eight days. After one week, the rock wool plugs with the small plantlets were transferred to hydroponics. The greenhouse conditions were 16 °C, 40% relative humidity, with a 16 h photoperiod (artificial light was provided when the outdoor light was less than 30,000 lux). Ten to fourteen days before harvesting, the greenhouse temperature was increased in some cases (experiments E1, E2, and LE2; see last paragraph in this section) to 22 °C at night (22.30 h–06.30 h) and 25 °C during the day (06.30 h–22.30 h).

A nutrient film technology (NFT) system was used for hydroponics. In this system, the rock wool plugs or the roots of the cuttings/plants were placed in plastic channels that were 5 cm deep, 15 cm wide, and as long as the cultivation tables in the greenhouse, i.e., 8 m. The plants were spaced at an average distance of 20 cm and the roots in the channels were covered with wecult® discs (Hermann Meyer KG, Rellingen, Germany). The channels were flooded with nutrient solution at varying intervals during the light period –2 x/h for 15 min for small plants, gradually reducing to 2 x/day for 15 min as the plants grew. The flow rate was 1.5 L/min.

The nutrient solution consisted of a 110:37:1 (by weight) mixture of YaraTera Kristalon scarlet/YaraTera Calcinit (Yara GmbH & Co. KG, Dülmen, Germany)/Ferty 73 Fe-DTPA (Planta, Regenstauf, Germany). The amount of nutrient was gradually increased during the cultivation, starting from a level that resulted in an electrical conductivity of 500 µS for the small plants at the beginning of the cultivation up to a level that resulted in an electrical conductivity of 1450 µS after about 4 months of cultivation. Electrical conductivity was measured twice a week and fertilizer in the above-mentioned mix was added to the nutrient solution to replace what the plants had consumed. In preliminary experiments, pH had been measured and did not change much (pH 7.7–7.9); therefore, we decided not to measure pH in the described experiments.

The following experiments were performed: E1 (October 2020–May 2021) and E2 (December 2021–June 2022) as large experiments in an 8.3 m^2 cultivation unit, experiments C1 (May–August 2019) and C2 (August–September 2020) with only a few plants (see Section 2.2 for details), and experiments LE1 (July–August 2022) and LE2 (September 2022–January 2023) (see Section 2.4 for details). Except for C1 and C2, where the fresh weight of the whole plants was measured during the experiment, roots were harvested at the end of each experiment and handled as described in Section 2.3.

2.2. Cuttings

When the soapwort plants had grown for three to four months, small rootlets began to form in the axils of lateral shoots. To propagate plants easily, cuttings were made from these lateral shoots by removing them from the mother plant and detaching the leaves from the bottom 10 cm of the stem. The top of the plant cutting was cut off, leaving only four leaves. The cuttings were placed with the emerging roots in water for two weeks. A small root system grew and the cuttings were then placed directly into the NFT system without any support.

In two experiments (Experiment C1 and C2), the growth of plants from seeds and cuttings was monitored for comparison. In the first experiment, seeds and cuttings (6 plants in each group) of cultivar S6 were used. Cuttings were prepared as described in the paragraph above. In the second experiment, seeds (8 plants) and cuttings (11 plants) of cultivar S3 were used. The fresh weight of the plants was regularly recorded; for the plants grown from seeds, the weight of the rock wool plugs was subtracted from the measured weight.

2.3. Root Harvest and Saponin Analysis

At harvest, plants were removed from the NFT system and the aerial parts were cut off. Roots were dried at 37 °C for 4–7 days, weighed (dry weight root), and prepared for SO1861 analysis as follows. Dry root material was ground to a fine powder and mixed with twenty times (v/w) 80% methanol, vortexed, and then extracted in an ultrasonic bath at 40 °C for 40 min. The extract was then centrifuged (4 °C, 30 min, 12,300 g). The supernatant was concentrated by evaporation overnight and then filtered through a 0.22 µm filter. The total volume of the sample was determined and exactly 1 mL was taken for analysis by ultra-high-performance liquid chromatography coupled to mass spectrometry (UHPLC-MS; Acquity UHPLC, Waters, Saint-Quentin, France) and quantified against a well-characterized standard of SO1861.

2.4. Lighting

Mostly, cultivations were performed using high-pressure sodium lamps (HPS) (Mastercolour CDM-T MW eco 360 W/842 E40, Philips, Eindhoven, The Netherlands). Two comparative cultivations (LE1 and LE2) were carried out between light-emitting diodes (LED; GP LED production DR/B 120 LB; Philips) and HPS. Plants (LE1: cultivars S3/S6; LE2: cultivar S3) of the same genotype and age were placed side by side under HPS and LEDs in the same NFT system. Details of plants and culture are given in Table 1. A 16 h photoperiod was used, with lights automatically switched on when a sensor at the top of the greenhouse measured a light intensity below 30,000 lux. The number of hours the lights were on was recorded.

Table 1. Cultivation parameters for comparative cultivation of plants using HPS or LED.

	Experiment LE1 (July–August 22) [1]		**Experiment LE2 (September 22–January 23) [2]**	
	HPS	LED	HPS	LED
Plant number	30 each		72 each	
Plant age at beginning [days]	70–90		0	
Plant cultivation [days]	62		147	
Cultivation size [m^2]	0.83		1.66	
Artificial light [h]	337.2		1962.6	

[1] Cultivation period LE1 (summer); [2] cultivation period LE2 (autumn/winter).

2.5. Cost Data Collection and Cost Analysis Model

All cost and underlying parameter values refer to a research greenhouse at Fraunhofer IME in Aachen, Germany, where all cultivation was carried out. The costs of the different factors in the SO1861 production process were determined by measurement and estimation. Specifically, the time needed for necessary work was clocked during all phases of the cultivation (start, ongoing cultivation, and harvest), electricity consumed by the lighting and pumping system was directly measured as were the amounts of fertilizer and water added to the system and the waste water removed from the system. For heating and cooling, the total annual costs of the greenhouse in 2021 were divided by 12 months and by the total cultivation area of the research facility greenhouse, measured in square meters. This provided an estimation of the average monthly heating and cooling costs per square meter. This information was used to calculate the costs for the chamber used, with an 8.3 m^2 cultivation unit. It was assumed that the heating and cooling costs would be evenly distributed throughout the year, and no seasonal variations were factored into the calculations. The electricity consumed by the lighting and the pump to transport the nutrient solution from a reservoir under the cultivation table to the NFT system was measured using an energy meter. The amount of water and fertilizer used was measured and the cost of acquisition/waste was calculated. The time spent on each task (e.g., planting and harvesting) was observed and labor costs were calculated on an hourly basis using the German minimum wage for 2021 (EUR 9.55), excluding employer contributions, as these vary depending on the type of employment ('mini-job', implying minimal employer contributions, or full-time employment). These data were integrated into a cost model developed in a spreadsheet program (e.g., Microsoft Excel). The model incorporated key variables such as root dry weight and SO1861 content measured in the dry roots, cultivation time, labor costs, and electricity consumption. To make the cost calculation more easily adaptable to new scenarios, units were defined for each cost position, i.e., kWh for electricity, hours for work time, or liters for water. Using this model, we estimated the impact of changes in critical parameters—such as propagation methods or lighting conditions—on the total production costs and production outcomes, under a standardized set of assumptions. The estimations were performed using a one-factor-at-a-time (OFAT) analysis, in which only one variable was adjusted at a time while all other variables were held constant [13]. This approach allowed for a precise assessment of the individual influence of each parameter on the outcomes. The analysis assumed constant unit costs and cost factors, with no external changes to other variables throughout the evaluation.

3. Results

3.1. Cost Data Collection

A large experiment (E1) with 189 plants (cultivar S3) in an 8.3 m^2 cultivation unit over seven months provided a complete set of data (Table 2). Excluding investment costs, the total cost was EUR 4490.46 to produce 1270 g of dry root biomass containing 12.7 g of SO1861. This corresponds to a cost of EUR 3.54 per gram of dry roots and EUR 353.58 per gram of SO1861. In particular, energy costs (lighting, cooling, heating, and water pumping) accounted for the largest proportion of costs (79.65%), with costs for lighting being the largest part of the total costs (39.15%), while the water and waste water costs (0.18%) and fertilizer costs (0.19%) were relatively low.

Table 2. Observed costs for an 8.3 m^2 cultivation (E1) with 189 plants, cuttings, and high-pressure sodium (HPS) lamps over 7 months.

Cost Element	**Unit**	**Unit Costs (EUR)**	**Units Required**	**Total Cost (EUR)**
Labor (start and end) [1]	hour	9.55	10	95.50
Labor during cultivation	hour	9.55	84	802.20
Fertilizers	month	1.20	7	8.40
Water/waste water (beginning and end) [1]	m^3	6.60	0.5	3.30
Water/waste water during cultivation	m^3	6.60	0.7	4.62
Lighting	kwh	0.17	1477	1757.63
Heating	kwh	0.08	10,304	772.80

Table 2. *Cont.*

Cost Element	Unit	Unit Costs (EUR)	Units Required	Total Cost (EUR)
Cooling	kwh	0.17	10,399	1035.30
Water pump	kwh	0.17	63	10.71
Total costs				4490.06

[1] Start and end refers to the preparation of the system and cuttings and to harvesting of the plants and cleaning the system; these cost factors are independent of the cultivation period and are therefore shown separately.

3.2. Cuttings or Seeds

In both experiments C1 and C2, where plants grown from seeds were compared with plants grown from cuttings for biomass accumulation, plants grown from cuttings accumulated more biomass in the given time. In a direct comparison (Figure 1), seedlings took approx. a month longer to grow to the same fresh weight as cuttings.

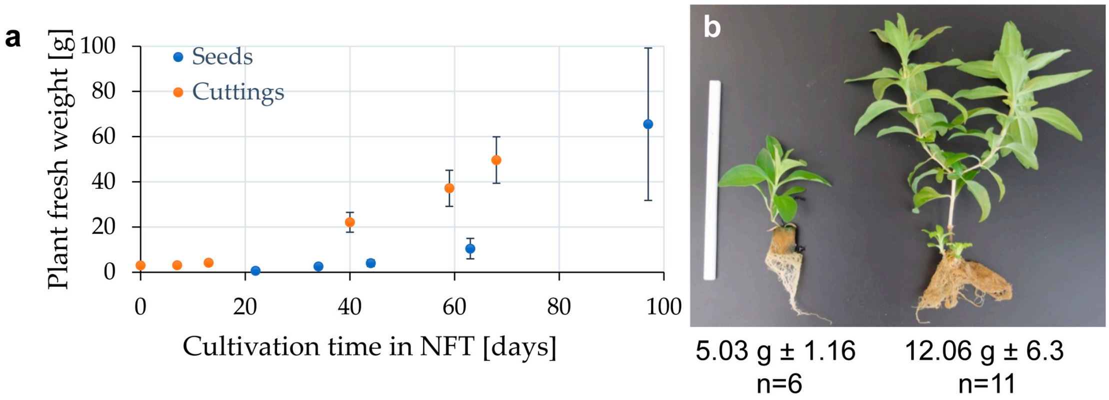

Figure 1. Comparison of plant growth from seedlings and from cuttings. Germinating seeds were placed on rock wool plugs while cuttings were placed directly in NFT without any support. (**a**) Experiment C1, cultivar S6: fresh weight was regularly recorded for 68 days for cuttings (orange dot; the aerial parts had to be cut off at this point as the plants were top-heavy and started to fall over) and 97 days for seedlings (blue dot). The fresh weight of seedlings after 44 days in NFT is approx. the same as the fresh weight of cuttings after 13 days in NFT. Mean/standard deviation is shown, n = 6; (**b**) experiment C2, cultivar S3: plant grown from seedling (**left**) and plant grown from cutting (**right**) after 30 days in NFT. The largest plant in each group is shown. Mean/standard deviation and group size are given below the image. A Kruskal–Wallis test showed that the median weights of the cuttings were significantly higher than those of the seeds (χ^2 (1) = 8.205, p = 0.0042) at the time point shown (30 days in NFT). White bar: 20 cm.

It was also found that the seeds of the soapwort cultivars used were not genetically uniform. To distinguish more clearly between plants with different genetic backgrounds, plants derived from the same seed (via cuttings) were defined as 'line'. All lines mentioned in this text (L1, L2, L3, L4, L5, L9, L16, L18, L27) were derived from cultivar S3. The use of cuttings makes it possible to use genetically uniform plants with desired characteristics (i.e., good growth, high production of SO1861), which is not possible with seeds of a mixed genetic background. It was also noticed that seedlings were more susceptible to damage and death (two seed-derived plants died in the experiment with cultivar S3) than cuttings. This is another good reason to use cuttings whenever possible, as they are more robust.

3.3. Root Biomass Accumulation

Plants of different lines differed in the accumulation of root biomass. In two different experiments (E2, LE2) where lines L3, L4, and L9 were compared, the root biomass of L9 was significantly lower than that of L4 (Table 3). In the three experiments shown, L4 produced on average 33% more dry root biomass; using cuttings from L4 plants would therefore reduce the cost per gram of SO1861.

Table 3. Accumulation of root biomass in different lines of cultivar S3.

	6 Months' Cultivation (E2)	5 Months' Cultivation HPS (LE2)	5 Months' Cultivation LED (LE2)
Line 3	4.76 ± 1.72	4.55 ± 1.42	4.07 ± 1.81
Line 4 *	5.82 ± 1.24	5.09 ± 1.54	5.08 ± 1.72
Line 9 *	4.27 ± 0.98	4.16 ± 1	3.59 ± 1.34

Means ± SD of root dry weight [g]. The 6-month cultivation (E2) took place from December 2021 to June 2022 (with HPLS); n = 10; the 5-month cultivations took place from September 2022 to January 2023 (LE2 with LED or HPS); n = 17. * Significant difference (p = 0.05).

3.4. SO1861 Content

During the trials, it became apparent that the amount of SO1861 produced in plants grown from different seeds of the same cultivar could vary dramatically. There were some plants that produced no measurable amount of SO1861, while the highest level measured was 1.49% weight/dry weight (w/dw). In the absence of the pre-selection of plants, it is likely that a certain percentage of plants will be non-producers of SO1861, which would increase costs.

Plants from the same line either all produced SO1861 or none. SO1861-producing/non-producing plants could not be distinguished by any other means than the actual elaborate measurement of the saponin (see Figure S1). Similar to root biomass accumulation (see Section 3.3), using cuttings from plants that produce a lot of SO1861 can significantly increase production at the same cost, i.e., reduce the cost per gram of SO1861 produced.

3.5. Light Comparison

Plants grown in parallel with HPS and LEDs (experiments LE1 and LE2) showed no significant differences in root biomass or SO1861 content in the roots (Table 4). However, the energy consumption of the two light sources was very different, with LEDs using 86%/81% less energy than HPS (LE1/LE2). In both light experiments (LE1/LE2), it was noted that the SO1861 content was much lower than in experiment E1; both plants grown with HPS and LEDs accumulated only about 0.2% w/dw SO1861 compared to 1% w/dw SO1861 in experiment E1 (see Section 3.1).

Table 4. Comparison of roots grown with HPS and LEDs.

	Experiment LE1 (July–August 22) [1]		Experiment LE2 (September 22–January 23) [2]	
	HPS	LED	HPS	LED
Root fresh weight [g]	902.8	885.8	1406	1847.5
Root dry weight [g]	83.9	82.3	330	317.8
SO1861 content [mg]	162	182	634	626
Energy used [kWh]	318.9	44.9	2783.8	522.8

[1] n = 30 (LE1); [2] n = 72 (L2).

3.6. Combination of Cost Factors and Cost Calculation Tool

Factors such as the genetic make-up of the plants, the method of propagation, and the light source have been shown to influence the costs of producing SO1861. These influences, studied in small-scale experiments (C1, C2, E2, LE1, LE2), were used to calculate their potential impact on experiment E1 mentioned above. For each factor, a scenario was calculated as well as a combination of all favorable aspects, i.e., a best-case scenario. All these virtual calculations are presented in Table 5, with the observed costs from experiment E1 in the first column as a reference point.

Table 5. Cost calculation of different cultivation scenarios for soapwort in a greenhouse hydroponic system.

		Scenario		A	B	C	D	E	F	G	H
			Observed Costs [E1]	**Seeds**	**Large Biomass**	**75% Producing**	**Large Concentration**	**LED**	**Best Case**	**Commercial (LED)**	**Commercial (HPS)**
Assumptions	Propagation		cuttings	seeds	cuttings	cuttings	cuttings	cuttings	cuttings	cuttings	cuttings
	Cultivation [months]		7	8	7	7	7	7	7	7	7
	Dry roots [g]		1270	1270	1480	1270	1270	1270	1480	3810	3810
	SO1861 content [g]		12.7	12.7	14.8	9.5	15.9	12.7	18.5	38.1	38.1
Cost elements	Start	Labor	EUR 95.50	EUR 95.50	EUR 95.50	EUR 95.50	EUR 95.50	EUR 95.50	EUR 95.50	EUR 286.50	EUR 286.50
		Seeds and support		EUR 24.70							
		Water and waste	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30	EUR 3.30
	Cultivation	Labor	EUR 802.20	EUR 916.80	EUR 802.20	EUR 802.20	EUR 802.20	EUR 802.20	EUR 802.20	EUR 2406.60	EUR 2406.60
		Fertilizer	EUR 8.40	EUR 9.60	EUR 8.40	EUR 8.40	EUR 8.40	EUR 8.40	EUR 8.40	EUR 25.20	EUR 25.20
		Water and waste	EUR 4.62	EUR 5.28	EUR 4.62	EUR 4.62	EUR 4.62	EUR 4.62	EUR 4.62	EUR 13.86	EUR 13.86
		HPS light	EUR 1757.63	EUR 2008.72	EUR 1757.63	EUR 1757.63	EUR 1757.63				EUR 5272.89
		LED light						EUR 371.28	EUR 371.28	EUR 1113.84	
		Heating	EUR 772.80	EUR 883.20	EUR 772.80	EUR 772.80	EUR 772.80	EUR 772.80	EUR 772.80	EUR 772.80	EUR 772.80
		Cooling	EUR 1035.30	EUR 1183.20	EUR 1035.30	EUR 1035.30	EUR 1035.30	EUR 1035.30	EUR 1035.30	EUR 1035.30	EUR 1035.30
		Fertilizer pump	EUR 10.71	EUR 12.24	EUR 10.71	EUR 10.71	EUR 10.71	EUR 10.71	EUR 10.71	EUR 32.13	EUR 32.13
Calculation	Total costs		EUR 4490.46	EUR 5142.54	EUR 4490.46	EUR 4490.46	EUR 4490.46	EUR 3,104.11	EUR 3104.11	EUR 5689.53	EUR 9848.58
	Costs per gram of SO1861		EUR 353.58	EUR 404.92	EUR 303.50	EUR 471.44	EUR 282.86	EUR 244.42	EUR 167.84	EUR 149.33	EUR 258.49
	Difference to observed costs			EUR 51.34	EUR 50.08	EUR 117.86	EUR 70.72	EUR 109.16	EUR 185.74	EUR 204.25	EUR 95.09
	Difference in percent			14.5%	−14.2%	33.3%	−20.0%	−30.9%	−52.5%	−57.8%	−26.9%
	Cost factor			1.15	0.86	1.33	0.80	0.69	0.47	0.42	0.73

The observed costs in the first column are derived from an 8.3 m^2 soapwort cultivation run for 7.5 months with 189 plants grown from cuttings (E1). Scenarios A to F are calculations based on this large cultivation and data from smaller/shorter cultivations and the cost-relevant factors identified in them. Seeds and support costs include the price for 400 seeds and rock wool plugs for 189 plants. Scenarios G-H are a virtual translation of the observed costs into a commercial greenhouse facility in terms of area under cultivation. Note that any other scenario can be calculated using the Excel spreadsheet provided as Supporting Data Model S1. Scenarios: A: seeds used for cultivation instead of cuttings; B: 33.3% (+423 g) more root biomass produced; C: 25% of plants are SO1861- non-producing plants; D: 25% higher SO1861 concentration in dry roots; E: LED lights used; F: best case: combination of scenarios B, D, and E; G: commercial greenhouse area with LED lights; H: commercial greenhouse area with HPS lamps. Blue cells: propagation method used, orange cells: cultivation period, purple cells: amount of dry roots expected, yellow cells: amount of SO1861 expected in dry roots. Dark gray cells in the calculation show the total estimated cost. Red indicates an increase, green a decrease in cultivation costs compared to the costs observed in the cultivations.

In detail, the costs changed as follows: In E1, cuttings were used; by using seeds instead of cuttings, the production costs would increase by 15% to EUR 5143 or EUR 405 per gram of SO1861 (scenario A in Table 5). Root biomass accumulation varied between plants—in two small-scale experiments (E2, LE2), we measured a significant difference in root biomass between L4 and L9, averaging 33%. There is no information on the dry root biomass accumulation of the plants used in E1; we assumed that the large mixture of plants would have a root biomass accumulation midway between the two lines. As a tendency, this assumption is supported by the root biomass accumulation of eight lines (Table S1) in the E2 crop. Therefore, using only cuttings of L4 would increase the root biomass by 16.5%, resulting in a 14.3% reduction in the cost per gram of SO1861 to EUR 304 (scenario B in Table 5).

In the absence of the pre-selection of plants, it is likely that a certain percentage of plants will be SO1861 non-producers, meaning that less SO1861 will be produced at the same price. Here, it is assumed that only 75% instead of all cultivated plants produce SO1861; the cost per gram of SO1861 would then increase by 33.3% to EUR 471 (scenario C in Table 5).

Using cuttings from plants that produce a lot of SO1861 can significantly increase production at the same cost, i.e., reduce the cost per gram of SO1861 produced. Based on an average production of 1% w/dw SO1861 in experiment E1 and the highest measured SO1861 value (1.49% w/dw), we assumed a 25% increase in SO1861 production by using cuttings from plants that are high SO1861 producers. This would reduce the cost per gram of SO1861 by 20.0% to EUR 283 (scenario D in Table 5).

Switching from HPS to LEDs significantly reduces energy consumption, cutting costs by 30.9% to EUR 244 per gram of SO1861 (scenario E in Table 5).

While some of the cost factors observed and mentioned above may seem too small to be relevant (e.g., root biomass accumulation; 2.3), the effect of combining all the cost optimizations mentioned shows the true potential for cost savings. As a best-case scenario, it was calculated that growing soapwort with LEDs and cuttings from plants producing 16.5% more biomass with 25% higher SO1861 concentration would reduce the production costs by 52.5% to EUR 168 per gram of SO1861 (scenario F in Table 5) compared to the costs observed in E1.

Other scenarios are conceivable and similar calculations for other crops, metabolites produced, and production facilities will yield different costs. For a quick check of the production costs, we have included the cost calculation tool based on the data from this publication (Supporting Data Model S1), which is an easy-to-use Excel spreadsheet that can help to identify the key cost drivers in greenhouse hydroponic plant cultivation.

4. Discussion

In this study, we have calculated the production costs of a specific saponin, SO1861, in the roots of soapwort cultivated hydroponically in a greenhouse. The analysis was aimed to address the economic feasibility of such systems and identify cost-effective factors in the production of plant metabolites like SO1861. In line with previous studies, we found that some cost items played a very small role and were, therefore, almost irrelevant (e.g., water and fertilizer) [14,15]. Factors that had a larger influence on production costs can be assigned to two different categories, related to a) the cultivation technique/equipment and b) the inherent characteristics of the plants (Table 6).

Table 6. Observed cost factors that can be easily optimized to reduce the total cost of SO1861 production in roots of soapwort grown hydroponically cultivation in a greenhouse.

Cost Factor	Description	Impact on Costs
Plant genetics	Plants produce no SO1861 Plants produce different amounts of SO1861 Plants produce different amounts of root biomass	Decrease in SO1861 production at same price
Propagation	Plants grown from seeds need longer to accumulate a given amount of root biomass than plants grown from cuttings	Using seeds lengthens the cultivation period, thus increasing the cost per gram of SO1861
Lights	LEDs use less energy than HPS	Using LEDs decreases energy costs, thus decreasing the cost per gram of SO1861

The use of LEDs instead of the more energy-consuming HPS is an example of the former, while the pre-selection of good SO1861-producing plants belongs to the latter category. Although saponins are important plant defense molecules [16], some soapwort plants produced almost no SO1861; for the plants, SO1861 appears to be just one saponin among many and not crucial for survival or reproduction [17]. In the greenhouse, SO1861-non-producing plants were observed in both cultivars used (S3 and S6). Furthermore, such SO1861-non-producing plants were also used in commercial field crops as we analyzed harvests from Poland and France that were virtually free of SO1861 (Figure S2). The selection of plants that are both good biomass producers and contain a maximum amount of the compound of interest (here: SO1861) has already been highlighted in a similar study [18]. The assumptions we have made about potential increases in root biomass production and SO1861 production are based on our current data, but are still a rough estimate. This is a weakness; however, this study is not intended to be an exact blueprint for similar work, but rather an attempt to identify factors with potential to improve cost-efficiency, and their order of magnitude. While the factors will be similar for other crops, their actual impact will be different. To address this fact, the cost model (Supporting Data Model S1) enables case-by-case calculations. While there are many studies on medicinal plant cultivation in hydroponics [19], we could only find one that looked into the agro-economic aspects [18]. However, given the increasing importance of the sustainable and reproducible production of secondary plant metabolites, hydroponic cultivation of medicinal plants in greenhouses will obtain more important and even rough cost calculations, as enabled by our cost model, that will be helpful to estimate the challenges and possibilities of other, similar projects.

The use of LEDs instead of HPS leads to a significant reduction in cultivation costs. This has been shown previously [20], but as shown before in the same report, LEDs generate less heat and therefore require slightly more energy/cost to maintain a constant temperature. Such small shifts in heat (i.e., energy) could not be detected in our study, but this should be considered in future studies.

With regard to lighting, heating, and cooling, it should also be considered whether year-round cultivation is necessary or whether a shorter cultivation period is possible and could be implemented in a cost-effective period of the year. The greenhouse used here is at a latitude of 51°, which means that there is a significant difference in day length between winter and summer. Most of the cultivations that we analyzed for the data presented here happened in the period September to May, when the average time of lamp use is 402 h/month. If the same cultivation had taken place in the March to September period, the average time of light use would have been 213 h/month, i.e., the lighting costs would have been halved. The cultivation of plants in NFT is largely self-sufficient, but labor is required at the start of cultivation (preparing the nutrient tank, making cuttings) and at harvest (removing plants from the system, cutting roots off, cleaning the system). In addition, the fertilizer concentration in the nutrient tanks needs to be measured and adjusted regularly. This was performed manually in our systems, but automation is common in other systems and would save costs. Also, some stress in the form of injury/drought and/or pruning of the aerial parts seems to be necessary for high levels of SO1861 in the roots, as the plants were treated in this way in all cultivations except the two light comparison experiments; in these two experiments, the SO1861 levels were exceptionally low. The increase in triterpenoid saponins in plants in response to stress has been observed before [21]. Furthermore, it seems that the production of secondary metabolites in plants is often increased by stress [22]. It was estimated that stress application to the plants in the cultivation described here could be performed in 12 h/month. Careful evaluation of any adapted stress-inducing protocol for its influence on both root biomass and SO1861 content would be necessary to validate such a protocol.

This study was conducted in a greenhouse designed for research and not for commercial crop production. Therefore, the size of the cultivation unit (8.3 m^2) within a greenhouse chamber (30.2 m^2) was small (27.5%)—in commercial greenhouses, the cultivation area is 80–90% of the total area [23], i.e., approximately three times larger. In a commercial greenhouse, therefore, three times as many plants could be grown with more lamps, nutrient solution, and labor for the same heating/cooling costs. As the lamps—if LEDs are used—account for only 12% of the cost, this would reduce the cost per gram of SO1861 by 57.8% (26.9% for HPS; scenarios G and H in Table 5). Given that the plants do not exceed a height of 40 cm with regular pruning, and that LEDs have been shown to have no negative effect on SO1861 production, a shelving arrangement with plants on several levels, e.g., a kind of vertical farm, could be set up. Such an arrangement would have the advantage of utilizing the available space more efficiently, enabling the cultivation of a greater number of plants within the same area, i.e., optimal use of space, which would further reduce energy costs. Cultivation of the medicinal plant *Euphorbia peplus* for the production of ingenol mebutate, a diterpene ester, has been successfully performed on four levels in a vertical hydroponic shipping container [18], so this type of cultivation should be feasible for soapwort. Shelf cultivation requires more lighting and potentially more cooling/ventilation compared to traditional greenhouse cultivation methods, due to the increased density of plants in a confined space, which reduces airflow and ventilation [24], but this could still be a more economical setup than a single-level cultivation.

It should be noted that the cost estimates provided in this analysis are specific to cultivation in Germany. Considering that energy and labor costs are the main factors influencing the production costs of SO1861, and that both are affected by geographical location, producers could explore the possibility of relocating to lower-cost regions, but moving production further afield would increase transport costs and could also result in additional expenses due to taxes or dealing with import restrictions if the chosen cultivation location is outside the EU.

5. Conclusions

This study demonstrated that the production costs of a saponin for pharmaceutical use obtained by hydroponic cultivation of soapwort plants in greenhouses depends on the genetic make-up of the plants. As the saponin in question, SO1861, is not produced by all plants, it is crucial to assess the phenotypes of the plants beforehand to ensure that they have the capacity to produce the desired saponin. In addition, the use of LED lighting and propagation by cuttings has shown significant benefits in terms of cost reduction. Reducing the production costs is directly equivalent to improved sustainability as either less energy or less material is used to achieve the same outcome. Replication and testing of the here-described cultivation practices in a commercial greenhouse are advisable to strengthen the still slim body of knowledge, particularly when pharmaceutical applications move closer to clinical use. All of this knowledge may inform the cultivation of other medicinal plants in the greenhouse, a practice that will become more common due to the protection of natural habitats and the need for reproducible biological production systems for, e.g., the pharmaceutical industry.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/horticulturae11040353/s1, Figure S1: SO1861 producers versus non-producers; Figure S2: absence of SO1861 in commercially available roots; Table S1: Accumulation of root biomass in different lines of cultivar S3; Model S1: interactive table for cost calculation of hydroponic greenhouse cultivation.

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Abbreviations

The following abbreviations are used in this manuscript:

CoG	Cost of goods
HPS	High-pressure sodium lamps
LED	Light-emitting diodes
NFT	Nutrient film technology
SO1861	Triterpenoid saponin SO1861

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