Elsevier Editorial System(tm) for Food Chemistry

Manuscript Draft

Manuscript Number: FOODCHEM-D-17-04214R1

Title: AROMA PROFILE DESIGN OF WINE SPIRITS: MULTI-OBJECTIVE OPTIMIZATION USING RESPONSE SURFACE METHODOLOGY

Article Type: Research Article (max 7,500 words)

Keywords: wine spirits; multi-objective; response surface; desirability; volatile compounds; distillation strategies

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Abstract: Developing new distillation strategies can help the spirits industry to improve quality, safety and process efficiency. Batch stills equipped with a packed column and an internal partial condenser are an innovative experimental system, allowing a fast and flexible management of the rectification. In this study, the impact of four factors (heart-cut volume, head-cut volume, pH and cooling flow rate of the internal partial condenser during the head-cut fraction) on 18 major volatile compounds of Muscat spirits was optimized using Response Surface Methodology and Desirability Function approaches. Results have shown that high rectification at the beginning of the heart-cut enhances the overall positive aroma compounds of the product, reducing off-flavors compounds. In contrast, optimum levels of heart-cut volume, head-cut volume and pH factors varied depending on the process goal. Finally, three optimal operational conditions (head off-flavors reduction, flowery terpenic enhance and fruity ester enhance) were evaluated by chemical and sensory analysis.

Prof. Stephen Elmore

Food Chemistry

11/13/2017

Dear Prof. Elmore,

I hereby resubmit the manuscript with the reference number **FOODCHEM-D-17-04214** and title “AROMA PROFILE DESIGN OF WINE SPIRITS: MULTI-OBJECTIVE OPTIMIZATION USING RESPONSE SURFACE METHODOLOGY” to be considered for publication in **Food Chemistry.**

We have carefully analyzed the recommendations of the reviewers and have taken into account most of them, as you can see in the itemized list of changes addressing reviewer comments included with this letter. Changes due to the recommendations of the editor and reviewers are answered in red.

We appreciate the time and dedication of the referees that helped us improve the readability of our manuscript.

Sincerely yours,

Francisco Lopez

Reviewers' comments:

Editor:

Please include linear retention indices (relative to straight-chain alkanes) in Table 2.

We added Table S1 to supplementary information with kovats retention indices and other information of the reagents requested by other reviewers. Table S1 is presented in lines 176-177.

Reviewer #1: (Yellow shadow)

The English is poor and needs to be improved. There also is an opportunity to include some more telling figures, which would be 2D projections or 3D surface plots of the 4D RSM model especially with the 2 most important factors.

After taking into account most of the reviewers' recommendations, the article has been reviewed by a native specialist.

We haven't introduced more Figures due to the limitation of the number of Figures by the journal style. Nevertheless, we have generated a supplementary file to relocate or create new figures and tables.

Since there are a large number of compounds, Figure S2 explains how the regression results can be quickly interpreted by using contour plots. The presentation of this figure is shown in **lines 337-339**.

A schematic of the distillation apparatus should be provided in the manuscript.

In the new version, Figure 1 has been changed for a schema of the distillation apparatus according to the reviewer´s recommendation.

A CCD is composed of a FFD (full factorial design and NOT a fractional factorial design).

We have corrected the mistake according to the reviewer´s comment in **new lines 88-91**.

The description of the blocking variable is poorly written L. 205. Is the blocking variable set to 1 for the first 10 measurements and 0 for the other 20 measurements? I am also not sure how 20 measurements fits a 4 factor CCD but I will read further.

We have rewritten the section according to the reviewer´s comment for better understanding (see **new lines 211-216**).

Answering your question, 40 experimental points were extracted from the 20 experimental assays, because we analyzed 2 heart fractions (heart-1 and heart-2) for every assay; see **211-216**. Therefore, this study leads to 30 data points (without counting central point replicates) and to 16 regression constants (counting the blocking variable). As a polynomial equation, the degrees of freedom can be calculated as N – K – 1, were N are the data points and K the regressions constants. Consequently, models have at least 13 degrees of freedom (without considering the analysis of variance, which reduces the regression constants to be estimated, and without considering the central point replicates).

Equation 1, seems to be full what terms were eliminated as non-significant effects. Should include the lack of Fit for the full model and the reduced model. Best way to represent the lack of fit is as an R2 value.

We have introduced Table S2 in supplementary information with different regression parameters, including the correlation coefficients of all full models (R^2) (**lines 336-349**) according to reviewer´s request.

L297 Propanol is not a terpenic compound.

We have rewritten the paragraph according to the reviewer´s comment, correcting the mistake (**new line 308**).

L370 If pH had a positive coefficient than low pH should actually lower the concentrations of ethyl acetate and acetal.

Perhaps, pH was not encoded in the experimental design but hydrogen ion concentration?

We have corrected the mistake according to the reviewer´s remark (**new line 396**).

We did not quite understand the question. pH was encoded as pH 3.2 = 1, pH 2.45 = 0 and pH 1.7 = -1 (see Table 1).

The quadratic model had 15 correlative terms and the design had 15 data points ignoring the center point replicates so I am a little concerned about the reproducibility of their findings. The best fit will always occur at the center point, it would be best if some other replicates were included in the RSM.

We have introduced the explanation in the paper (**new lines 211-216**). See also the previous explanation.

Some of the tabular concentrations are reported with too many significant digits. The standard deviation should never have more than 2 digits.

We have worked with three significant figures with all concentration data. The standard deviations maintain the same number of decimals as their respective concentration.

bloc is misspelled

We have corrected the mistake according to the reviewer comment.

(CFR) should appear immediately after cooling flow rate, L. 103.

We have followed the recommendation of the reviewer (**new line 101**).

We want to thank reviewer #1 for all the considerations and contributions for the improvement of the work.

Reviewer #2: (Green shadow)

This manuscript describes the development of new distillation strategies aimed at improving the quality, safety, and process efficiency of the distillation process.

The aim of the study was to find operational conditions to obtain specific organoleptic characteristics for a Muscat wine spirit. The operation factors that were considered were (1) HTV, (2) HDV, (3) pH, and (4) CFR. The effects of these factors on 18 compounds were evaluated.

The topic is interesting and the scientific approach to investigating the hypothesis is sound. The paper is well written and the conclusions are clear. My only concern is that the manuscript is not a chemistry focused investigation, but rather more statistical of nature. I question whether Food Chemistry is the best fit for this article and would suggest that a statistically focus journal may be better suited for this manuscript.

Thank you for the comments about the paper. This study is actually a multidisciplinary work, which joins chemical engineering, sensory analysis and other sub-disciplines of food chemistry. In order to analyze the results of these fields, it is true that different statistical methods already described have been used. However, all these methodologies have been implemented to study a chemical process such as the distillation of spirits. Thus, we considered that this study is in accordance with the journal profile.

Here follows comments for the authors consideration:

1. The highlights do not accurately reflect the key findings of the study. I suggest changing the highlights to include which rectification process increased the flavor profile of the spirit products.

We have rewritten the highlights to include the reviewer´s recommendation.

2. I would caution the authors to refer to "quality" when discussing the improvements of the distillation processes. Quality is a difficult attribute to define without proper consumer and sensory studies. Keep the focus on the actual flavor and aroma profiles that were increased or decreased.

We have changed the word "quality" where it refers to our results (**new lines 25 and 79**), according to reviewer´s request. We have kept the word "quality" in cases where it was stated that producers "want to produce quality products" (**lines 18 and 36**).

Lines 26-27: This sentence doesn't make sense.

We have rewritten according to the reviewer´s comment for better understanding.

Line 45: Replace "halfway" with a better descriptive word.

We have changed halfway by “intermediate” according to the reviewer´s recommendation.

Lines 54-55: Fix references to Arrieta-Garay.

We have corrected the mistake in the references.

Lines 87-100: Give a reference to a statistical textbook or paper that describes CCD for the readers to reference if they are not familiar with the technique.

We have introduced a reference according to the reviewer´s recommendation.

Lines 101-103: The authors discussed in lines 76-80 that their key objectives are the investigate (1) HTV, (2) HDV, (3) pH, and (4) CFR, however, here they state that they are only considering HDV, pH and CFR in their 3-level-3-factor CCD.

Please remove the HTV from the list of factors that were investigated in lines 76-80.

We have rewritten **lines 101-103** to better explain why CCD was designed for 3 factors (20 experiments). However, each experiment that was analyzed had two heart fractions (heart-1 and heart-2) that were analyzed

Line 116: The pH levels selected for this study are very low. Give justification for the selected pH range.

The acidification of wine co-products to preserve them and to later obtain spirits has been previously reported in the literature (Lukić, Miličević, Tomas, Radeka, & Peršurić, 2012), however we did not find information about alkalinization. In addition, during preliminary studies, we had the hypothesis that the carboxylic acids would tend to esterify rapidly in a very acidic media, obtaining a very fruity spirit.

On the other hand, it would be also interesting to know the behavior of the congeners of wine at higher pH. We appreciate the comment, as it is a good idea to take into account alkalinization in future studies.

The justification has been included in **line 117**.

Lines 121-124: From first inspection of section 3.4 it is hard for the reader to see how the optimal conditions discussed in Section 3.4 shows the ideal pH range. The authors should be more specific in describing the selection of pH's for their distillates.

We have rewritten the paragraph according to the reviewer´s comment for better understanding.

Lines 134-135: Rephrase, the sentence doesn't make sense.

We have removed this line, because with the introduction of a schema of experimental device, it is not necessary.

Line 136: Covered with what? Did the authors use material that was inert and didn't scalp the volatiles from the headspace of the test tubes?

We have rewritten according to the reviewer´s comment for better understanding.

Line 217: Why did the authors not use Odor Activity Values? OAV would best describes the importance of a specific compound to the odor of the distillates. How does their modelling of the activity of the aroma compare to using OAV values. "Larger-The-Best" and "Smaller-The-Best" is not good English. Are these accepted terms for this type of modelling? If not I would suggest using other terms to better describe that a lower conc is the wanted outcome or that a larger conc of the compound is the ideal outcome for the distillate.

The use of OAV would not have changed the results or the methodology of optimization of the study, since only a ratio factor differentiates OAV and concentration. However, OAV may be easy to understand, so we will take into account reviewer #2 recommendations for future studies.

Regarding “Larger The Best” and “Smaller The Best”, these terms have been previously used by Costa, Lourenço and Pereira (2011), a widely cited review article (about 79 citations at 2017/10/26). Other authors have used other terms like “maximization” and “minimization”. We considered that “Larger and Smaller The Best” terms were more appropriate for our work.

Line 239: 17 assessors is a really small sensory group. Conclusions drawn from the sensory evaluation can only be discussed in terms of "suggested trends".

Although there is no formal consensus, we consider that characterization studies should be done with about 10 tasters or more. For example, in Statistics for Sensory and Consumer Science (2010) it is cited that that “A sensory panel will normally consist of between 10 and 15 trained assessors and be thought of as an analytical instrument” and “For consumer studies […] will use at least between 100 and 150 consumers“. In this study, we performed a characterization study to validate the chemical optimization by sensory analysis with 17 trained assessors. Then, taking advantage of the characterization study, we evaluated the sensory preferences of the panel.

We have introduced “suggested trend” into the discussion in lines **531-533,** according to reviewer´s request

Line 358: Rephrase sentence using correct grammar.

We have rewritten according to the reviewer´s comment for better understanding (**new lines 384-386**).

Line 373: "due to exhaustion"? Please rephrase and use an alternative to "exhaustion" throughout the text.

We have changed exhaustion to “depletion over time” according to the reviewer´s recommendation (**new line 399**).

The section on CFR seems out of place considering the experimental design discussed in Section 2.1 does not include CFR as part of the design matrix.

We do not quite understand the question of the reviewer #2; however, we consider that the effect of the CFR notably affects the composition in the heart as can be observed during the study.

There are no references to Nakama 2014 in the text. Remove from reference list.

We have corrected the mistake of the reference according to the reviewer´s comment.

Other comments:

* Don't start sentences with numbers, and don't start sentences with abbreviations.

We have rewritten some sentences according to the reviewer´s comment for better understanding.

We want to thank reviewer #2 for all the considerations and contributions for the improvement of the work.

Reviewer #3: (Blue shadow)

Goal of the study, study setup and analytical methods are clearly structured and well described. Discussion of the results is sound and detailed. There are only minor issues to be clarified, e.g. that in the abstract and the introduction, 18 major volatiles are mentioned (aside from ethanol), while in Table 4 geraniol appears, thus there are 19 volatiles listed.

Thank you for the comments about the paper. The main study was performed for 18 compounds, selected according to their presence in the Muscat wine of 2015 vintage. However, other compounds such as ethyl carbamate and geraniol were included in the calibration of the chromatographic analysis in case we observe interesting behaviors that could complement the study.

Regarding the results, geraniol was not quantified in Muscat wine of 2015. However, geraniol was quantified in the spirit of Muscat wine of 2016, and it has shown a tendency similar to linalool, and for that reason we have shown its values (see in new **lines 497-499** where its presence is explained).

For better understanding, in Table 4 we have changed n.c. by d.-n.q., we have rewritten **lines 174-175**, **lines 279-280** and we have included Table S1 in a supplementary file with reagents information according to reviewer request.

The author may consider to add a schematic sketch of the described "batch distillation column with an internal partial condenser".

We cannot introduce more Figures due to the limitation of the number of Figures by the journal style. Nevertheless, we have generated a supplementary file to relocate figures and tables. In the new version, Figure 1 has been changed for a schema of the distillation apparatus according to the reviewer´s recommendation.

Furthermore, used chemicals should appear as separate sub-section in section 2. It is also not clear whether for all 19 studied volatiles reference compounds were available as well as in which quality and where there were purchased (incompletely mentioned in line 173).

We have introduced Table S1 in supplementary information with kovats retention indices, CAS and supplier companies of the analytical reagents, and we have rewritten some sentences (**lines 176-178**) according to reviewer request.

Finally, there is some inconstancy with references. While there is no citation in the text of Nakama et al, there are three citations (Table 2) not listed in the references. And there are two references, which would fit to your citation "Y. Arrieta-Garay et al., 2014".

We have corrected the mistake of the reference according to the reviewer´s comment.

Last, but not least, it is recommended to carefully cross-check Tables 2 and 4 regarding stated significant differences ("a", "ab", "b", "c"). While in Table 2 "a" is used for the highest concentration, in Table 4 "a" is used for the lowest concentration.

We have changed the order of the sub- indices according to the recommendations of the reviewer

B) DETAILS:

Lines 30-31: Add "wine spirits" to the keywords

We have introduced the keyword wine spirits according to reviewer´s recommendation

Line 55: Change to "Y. Arrieta-Garay …"

We have corrected the mistake of the reference according to reviewer´s recommendation.

Line 203: Change to "blocking modifies the origin …"

We have corrected the mistake according to reviewer´s recommendation.

Line 223: Change to "compound below the …"

We have corrected according to reviewer´s recommendation.

Line 250: Add reference to "Latin square designs"

We have introduced a reference according to reviewer´s recommendation

Table 2: Ethyl acetate - heart-2 cut: shouldn't it be "c" instead of "b"?

We have reviewed the calculations and Tukey's HSD test after ANOVA ($p < 0.05$) indicated that there were no significant differences between Heart-1 and Heart-2, probably due to the large deviation of Head fraction.

Table 2: Footnote e: "2013" instead of "2012"

We have corrected the mistake of the reference according to reviewer´s recommendation.

Table 3: Foot note: Most likely it should be read like "* $p < 0.01$" and "** $p < 0.001$"

We have removed the p-value $p < 0.0001$ and have rewrote the title and footnote, according to reviewer´s recommendation for better understanding.

C) EDITORIAL REMARKS

1) There should be always a space between values and units according to ISO 80000-1:2009 (e.g. lines 161 and 318, etc).

We have corrected the mistakes in the text.

2) Reconsider to reduce capitalization throughout the whole submission (e.g. "French style" instead of "French Style", "heart-cut" instead of "Heart-cut", "axial points" instead of "Axial Points", etc).

We have followed the reviewer´s recommendation.

3) Mention always name, city and country of manufacturers/providers (e.g. lines 157, 158 and 165).

We have followed the reviewer´s recommendation.

We want to thank reviewer #3 all the considerations and contributions for the improvement of the work.

Reviewer #4: : (Magenta shadow)

The aim of this study was to determine operational conditions for a batch distillation column with an internal partial condenser to obtain different specific organoleptic characteristics for a Muscat wine spirit. Heart-Cut Volume (HTV), Head-Cut Volume (HDV), pH (adjusted with sulfuric acid) and Cooling Flow Rate of the internal partial condenser during the Head-cut fraction (CFR) were considered the main operational factors for improving the quality of the spirit. I think that presented results are very interesting for the scientists (working in the field of alcoholic beverages) as well as for the spirit producers. In my opinion the article is in the scope of Food Chemistry journal and should be published after minor correction.

Thank you for the comments about the paper.

Remarks:

l. 161 - why were the samples adjusted to 40% v/v of alcohol? How was it done?

The calibration method to quantify the different compounds in the GC-FID was established with synthetic solutions at the same alcoholic composition (40% v/v). We adjusted the samples to 40% ethanol to avoid matrix effects due to ethanol differences during sample injection in the GC. This is a common procedure for the analysis of hydro-alcoholic samples by direct injection. Samples were adjusted to 40% v/v by adding distilled water or ethanol absolute (HPLC-gradient).

We have rewritten **lines 164-165** for better understanding.

l. 164-174 - what volatile standards were applied for GC analysis?

We have introduced Table S1 in the supplementary information with kovats retention indices, CAS and supplier companies of the analytical reagents, and we have rewritten some sentences (**lines 177-178**) according to the reviewer's request.

l. 266 - The name of the paragraph 3.11 should be changed. It includes only the description and discussion of the results of concentration kinetics in Head and Tail fractions.

We have changed the tittle according to reviewer request.

l. 449 - "should clean the Heart-cut from head compounds" but linalool is not a head compound

In this multi-objective optimization (TEN), we wanted to maximize linalool concentration and minimize the concentration of head compounds. We have replaced "head compounds" to "acetaldehyde and ethyl acetate" for better understanding, according to the reviewer´s request (**line 475**).

l. 308 - how was ethyl carbamate evaluated? It is not clear.

We have introduced Table S1 in supplementary information with kovats retention indices, CAS and supplier companies of the analytical reagents, and we have rewritten some sentences (**line 178**) according to the reviewer´s request.

l. 589 - the name of the International Journal of Food Science and Technology, sometimes with "and" and sometimes with "&"

We have homogenized the reference list.

l. 605 - there is no number of journal nor pages for this reference

We have corrected the mistake.

Table 2 - where are the results of Tails fraction? There is no mentioned references in the References paragraph.

As the reviewer #4 says, it might be also interesting to study the Tail fraction. However, we find Tail fraction discussion unnecessary as the goal of this study was focused on obtaining organoleptic improvements in the Heart fraction, and the Tail fraction does not directly influence the Heart fraction composition. Nevertheless, we will take into consideration the idea of studying on distillation Tails in future studies.

We have corrected the mistake in the references chapter.

We want to thank reviewer #4 all the considerations and contributions for the improvement of the work.

Reviewer #5: (Grey shadow)

The present manuscript describes an optimization study of several factors affecting the composition of volatile constituents in wine distillates. More specifically, the authors examined the distillation of Muscat wine with a packed distillation column (in laboratory scale) with internal partial condenser and varied the levels of head-cut and heart-cut volume, pH of wine, and cooling flow rate. The collected fractions from distillation were analyzed for certain volatile compounds. Through experimental design, the authors aimed to find optimal distillation conditions for three different situations: to reduce the head compounds in the final product, to enhance the terpenic content and to enhance the ester (fruity) content of the final product. After finding the optimal conditions, they evaluated them with the distillation of two different types of wine and also they related the chemical data with sensory data for confirmation purposes.

The article in its current form is generally well written, sufficiently novel and worthy for publication in Food Chemistry.

Thank you for the comments about the paper.

However, there are some critical points described below about the experimental design that the authors should carefully clarify before acceptance:

Major points

1) The authors have used a central composite design with three factors (ie, Head-cut volume, pH and Cooling flow rate), consisting of 20 runs (6 of them were the central points). The relevant data are presented in Table 2 and discussed in section 3.1. Actually, the authors discuss only the data of center points as well as their RSDs. There is no statement either in the text or the table for important statistics of the design, such as lack of fit, residuals, the statistically important terms of the model as well as some sort of graphical representation, ie., response surface plots. Could the authors include them in the manuscript and if not, please explain the reason?

We have not introduced more Figures and Tables due to the limitation of their number by the journal style; nevertheless, we have generated a supplementary file with some new tables and figures according to the reviewer´s recommendation.

Since there are a large number of compounds, Figure S2 has been included in supplementary information to explain how Table 3 can be interpreted quickly by using contour plots. The presentation of Figure S2 is done in the **lines 339-340**.

We have introduced Table S2 in supplementary information with different parameters about goodness of fit (indicated in **line 338** in the full-paper) according to the reviewer´s request.

2) After running the 20 experimental runs, the authors added to the same design described above, one more factor, the Heart-cut volume, without performing additional experimental runs. I would like the authors to explain the reason for doing this instead of designing from the beginning a CCD with four experimental factors. In my opinion, this practice is not statistically sound.

It is true that performing a CDD with 4 factors with the same replicates (30 assays = 30 data points, in contrast with the current 20 assays = 40 data points) would improve the

consistency of the design; however, the philosophy of experimental design is often based on performing the minimum number of experiments to obtain the maximum amount of reliable information. We assumed that the interdependency of both hearts had a low influence in the study by performing 6 replicates of the central point.

3) The data from the response surface modelling are presented in Table 3 and discussed in section 3.2. Similarly to my 1st comment, although the authors present the coefficients of the model and their statistical importance, they do not provide the lack of fit of the regression. Furthermore, no graphical representation is given, which makes it very difficult for the reader to follow the discussion.

In the supplementary information, we have introduced the lack of fit test in Table S2 and we have also included an explanatory graph (Figure S2) for better understanding of Table 3; both are explained in lines 334-342

4) In Table 2, the odor threshold of terpineol is too high. I have found in the literature that it is ranged between 0.280-0.350 mg/L (see the attached pdf for the references). If this is true, then the authors should have included terpineol in the response surface model because its Heart-cut maximum value is higher than its odor threshold. This was the criterion for choosing the compounds for multi-objective optimizations (lines 425-428).

We have used the odor threshold of a-terpineol of 75 g/hL a.a. (300 mg/L) determined in a hydro-alcoholic solution of 40 % v/v (Cacho et al. 2012). Lower threshold levels have been published, but in aqueous conditions. We considered that the value of Cacho et al. 2012 was more adequate for our work, although it would be a good idea to verify it in future sensory studies.

5) Lines 474-478 and Table 4: the ratio of the analytical values of acetaldehyde in the two wines (of year 2016) are similar with the predicted ones. However, for ethyl acetate and fruity esters this is not true, as stated by the authors. Probably, the model does not perform well as regards the HOR strategy. I believe that the authors should have distilled in the optimal conditions for the three strategies applied, the same wine (Muscat 2015) used in the optimization study. In this manner, they would validate the response surface models by comparison of the predicted with the experimental values of volatile components. The distillation of other matrix (ie different wines) would be the next step. Do the authors have experimental data to support this?

As reviewer #5 said, the best way to validate the strategies was to use Muscat wine of 2015, but it has not been possible due to preservation problems. For this reason, the procedure was applied to a wine of the same variety and company, but of the following vintage, as well as Macabeu wine (without terpenic character), in order to validate the model. This fact will be taken into account in future research.

Minor points

These include some grammatical errors, missing part or format of a reference, etc and have been incorporated in the attached pdf file as comments that should be corrected.

We have corrected the following mistakes, indicated in the attached file according to the reviewer's comments:

Lines 54-55.

We have corrected the mistake in lines 54-55.

Lines 88-100. “It can be omitted as it describes the theory of CCD. Alternatively, give a reference for the theory of central composite designs”.

We maintain this part according to the comments of other reviewers, adding a reference.

Lines 104 and 105.

We have corrected the mistake of bloc to block.

In lines 115 and 123. “give molarity”.

We have changed the concentration specification according to the reviewer´s comment.

In lines 113, 117, 118, 153.

We have changed the mistake “alcohol degree” according to the reviewer´s request, introducing the official term: “alcoholic strength by volume”.

Line 125. “it would be very useful for the readers if you provided a photo or diagram of the laboratory scaled version distillate system in supplementary material.”

We have introduced a schema of the experimental device according to the reviewer´s request.

Line 166.

We have accepted the recommendations of reviewer to remove the word “chromatographic”.

Lines 171-172.

We have modified the phrase according to the reviewer´s advice: Column-head flow was initially set at 0.5 mL/min (28 min) and increased with a rate of 5 mL/min2 up to 1.1 mL/min (67 min) using helium as carrier gas.

Line 203.

We have corrected the mistake: modifies replaces modify.

Line 229 reviewer comment: “It would be better to put Figure 1 in supplementary material. No results of the study are presented.”,

We have moved Figure 1 to supplementary information.

Line 268.

We have changed “showed” by “presents” according to the reviewer´s advice.

In line 276 reviewer comments about ethyl octanoate: “its concentration is not statistically different between the head cut and heart cut 1. it seems to be an exception.”

It showed no statistical differences, but the general tendency is a diminution of the ethyl ester concentrations throughout the process.

Line 285.

We have corrected the mistake: levels was changed to level.

The reviewer comments for a-terpineol: the odor threshold referenced in table 2 is unreasonably high. The range is 0.250-0.350 mg/L,

We have used the odor threshold of a-terpineol of 75 g/hL a.a. (300 mg/L) determined in a hydro-alcoholic solution of 40 % v/v (Cacho et al. 2012). Lower threshold levels have been published, but in aqueous conditions. We considered that the value of Cacho et al. 2012 was more adequate for our work, although it would be a good idea to verify it in future sensory studies.

Line 316.

We have changed "revealed" to "was" according reviewer advice.

In lines 317-319: "Table 2 shows that relative standard deviations in the Head-cut were high, especially for ethyl lactate (28%), ethyl octanoate (38%), ethyl butyrate (40%) and ethyl hexanoate (44%)." Reviewer comments: "Please, rephrase as the RSDs are not presented in Table 2. But they can be calculated."

We have rewritten this paragraph according to the reviewer´s advice for better understanding.

In line 346 "larger HTV". Reviewer says "do you mean HDV?"

HTV is the correct term.

"Otherwise, I cannot understand the negative coefficients of both factors, ie HDV and HTV".

Extended explanation: If we increase the volume of the head-cut fraction, these compounds will accumulate in this fraction (head), and, therefore, their concentration will decrease in the next fraction (heart). On the other hand, increasing the volume of the heart fraction will increase the dilution of these compounds in this fraction (heart). For both reasons, these two factors have the negative coefficient.

We have modified paragraph **371-372** for better understanding.

Lines 358 – 361.

We have modified the phrase according the reviewer's advice (**new lines 384-386**).

Line 365

We have changed "acid" to "acidic" according to the reviewer´s advice.

Line 366

We have changed "Otherwise" to "Furthermore" according to the reviewer´s advice.

Line 386

We have changed "its" to "their" according to the reviewer´s advice.

Line 390

We have changed "these" to "this" according to the reviewer´s advice.

In lines 464-467: "Table 4 shows the predicted composition of Muscat 2015 wine

distilled with the calculated optimal conditions (RSM). In addition, this table shows the mean concentration, standard deviation and significant differences of Muscat and Macabeo 2016 wines distilled with the same optimal conditions." Reviewer comments: "I assume these are the concentrations in the Hear-cut fraction, ie the final product.... please, indicate it in Table 4 and rephrase lines 464-467..".

We have corrected text (lines 490-493) and Table 4 according to the reviewer's query.

Reviewer comments: Lines 474-478: The ratio of the analytical values of acetaldehyde in the two wines (2016) are similar with the predicted ones. However, for ethyl acetate this is not true. Probably, the model does not perform well as regards the HOR strategy."

Yes. It seems that HOR strategy does not perform well for ethyl esters (explained in lines 500-503).

Line 605.

We have corrected the mistake in the reference according to the reviewer´s request.

Reviewer comments: In table 2 reviewer demands specify "specify units....mg/L" in the odor threshold.

Units are the same for all concentration values (including odor thresholds) and are indicated in the footnote; nevertheless, we have better specified in the footnote according to the reviewer´s comment

Respect Figure 1 reviewer comments: "this figure should be omitted as it does not present any experimental data. It could be placed in supplementary material"

We have moved Figure 1 to supplementary information (Figure S1).

We want to thank reviewer #5 all the considerations and contributions for the improvement of the work.

Highlights

- High rectification during head fractions improves flowery and fruity spirit aroma
- Optimal pH and distillation cuts depend on aromatic profile goal
- Sensory analysis shows good correlation between aroma descriptors and chemical data

AROMA PROFILE DESIGN OF WINE SPIRITS: MULTI-OBJECTIVE OPTIMIZATION USING RESPONSE SURFACE METHODOLOGY

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Abstract

Developing new distillation strategies can help the spirits industry to improve quality, safety and process efficiency. Batch stills equipped with a packed column and an internal partial condenser are an innovative experimental system, allowing a fast and flexible management of the rectification. In this study, the impact of four factors (heart-cut volume, head-cut volume, pH and cooling flow rate of the internal partial condenser during the head-cut fraction) on 18 major volatile compounds of Muscat spirits was optimized using Response Surface Methodology and Desirability Function approaches. Results have shown that high rectification at the beginning of the heart-cut enhances the overall positive aroma compounds of the product, reducing off-flavors compounds. In contrast, optimum levels of heart-cut volume, head-cut volume and pH factors varied depending on the process goal. Finally, three optimal operational conditions (head off-flavors reduction, flowery terpenic enhance and fruity ester enhance) were evaluated by chemical and sensory analysis.

Keywords: wine spirits; multi-objective; response surface; desirability; volatile compounds; distillation strategies.

1. Introduction

One of the main challenges of the food and beverage industry is to obtain unique products in an increasingly competitive market. In the case of spirits, new operating strategies can aid to improve quality, food safety and efficiency of the distillation process. Batch distillation is the most used technique to produce spirits, where the distillate is collected in three consecutive fractions: head-cut (waste), heart-cut (product) and tail-cut (waste), to obtain a product with minimum off-flavors and toxic compounds. Traditional systems, like copper *Charentais* alembics (French style), produce drinks with high levels of volatile compounds that enhance their genuineness, an important feature of distinctive alcoholic beverages. However, alembics allow limited control of the distillation process to improve the

product. On the other hand, modern continuous columns are generally used to obtain spirits with a neutral aroma, intended for flavoring or ageing. In the spirits industry, batch columns (German style) represent an intermediate technique, which provides enhanced control of the rectification by varying the reflux rate; however, these systems are slow to respond, severely limiting the process flexibility. Many studies have reported the differences of the available spirits distillation systems (Alcarde, Souza, & Bortoletto, 2012; Christoph & Bauer-Christoph, 2007; Da Porto & Decorti, 2008; Madrera, Gomis, & Alonso, 2003; Porto, 2008).

An innovative experimental system is the batch packed column equipped with an internal partial condenser that allows fast and flexible control of the internal reflux rate (García-Llobodanin, Roca, López, Pérez-Correa, & López, 2011). This system has been compared with a traditional alembic by distilling wine and other fermented agricultural raw materials (kiwi, pear and grape pomace) showing significant differences (Arrieta-Garay et al., 2013; Arrieta-Garay, Blanco, et al., 2014; Arrieta-Garay, López-Vázquez, et al., 2014). In particular, high refluxes at early fractions removed acetaldehyde, ethyl acetate and acetal from the heart-cut, which allows obtaining a cleaner wine spirit (Matias-Guiu, Rodríguez-Bencomo, Orriols, Pérez-Correa, & López, 2016; Rodríguez-Bencomo, Pérez-Correa, Orriols, & López, 2016). Although packed columns increase distillation times and are difficult to control (García-Llobodanin et al., 2011), the variable internal cooling flow rate can quickly adapt the rectification level; hence, the producer can modify the volatile composition of the spirit throughout the process by specific operational strategies (Matias-Guiu et al., 2016).

The distillation of fermented beverages causes the reaction of several aroma compounds such as terpenes (Baxter, Laurie, & Mchale, 1978; Bedoukian, 1986; Ohta, Morimitsu, Sameshima, Samuta, & Ohba, 1991; Osorio, Pérez-Correa, Belancic, & Agosin, 2004), esters (Fischer & Speier, 1895), furfural (Mottram, 2007; Nakama, Kim, Shinohara, & Omura, 2014; Yemiş & Mazza, 2012) and aldehydes (Kłosowski & Czupryński, 2006), which undergo transformations in a hot acid media. It has been reported that the juice pH alters the

68 microbiological behavior during the fermentation, affecting the aroma composition of pear
69 and melon spirits (García-Llobodanin, Senn, Ferrando, Güell, & López, 2010; Gómez, Úbeda,
70 & Briones, 2008). However, there is no information regarding the influence of pH during the
71 distillation. Furthermore, the distillation behavior of each compound changes throughout the
72 process (Jouret, Cantagrel, & Galy, 1998).

73 The aim of this study was to determine operational conditions for a batch distillation
74 column with an internal partial condenser to obtain different specific organoleptic
75 characteristics for a Muscat wine spirit. Heart-Cut Volume (HTV), Head-Cut Volume (HDV),
76 pH (adjusted with sulfuric acid, a common technique used in marc storage (Lukić, Miličević,
77 Tomas, Radeka, & Peršurić, 2012)) and Cooling Flow Rate of the internal partial condenser
78 during the head-cut fraction (CFR) were considered to be the main operational factors. To
79 carry out the head-cut multi-objective optimization (18 compounds), Response Surface
80 Methodology (RSM) was applied by performing a Central Composite Design with face
81 centered axial points (Derringer & Suich, 1980). For the multi-objective optimization, the
82 Desirability Function Approach (Derringer & Suich, 1980) was used for the most relevant
83 volatile compounds of Muscat spirits. In addition, optimal strategies were sensory analyzed.

84 **2. Material and methods**

85 ***2.1. Central Composite Design (CCD)***

86 Design of experiments is widely used to unveil the impact of defined input process
87 variables (factors) on output process variables (responses). The CCD is a type of design of
88 experiments consisting of a 2-level full factorial design (FFD) with a center point and axial
89 points (Montgomery, 2013). The FFD is a design that studies the effect of all possible
90 combinations of 2 or more factors at 2 levels. Center point is an experimental run whose
91 factor values are the average of the two levels of the FFD factors; they are usually replicated
92 to estimate and improve the variance of the system. Axial points are experimental runs with

93 the same factor values as the center point, except for one factor whose value is at a given
94 distance (α) from the center point. Factor values are usually rescaled (coded): FFD points =
95 ±1, center point = 0, and axial points = ±α (one factor) and 0 (the other factors). Thereby,
96 CCD results allow a statistical estimation of linear and quadratic effects on a given response
97 with a reduced number of experiments.

98 For this study, a 3-level-3-factor CCD with face centered axial points (α = 1) and six
99 replicates of the center point was designed (20 runs). Factors were Head-Cut Volume (HDV),
100 pH and Cooling Flow Rate (CFR) of the internal partial condenser of the column. To
101 minimize the number of runs, the factor HTV (Heart-Cut Volume) was not considered;
102 however, HTV was considered with the RSM, since 2 heart cuts were obtained from each
103 experiment. Runs were ordered with a randomized 2-block design to enhance the reliability
104 and validity of the statistical analysis of the factor effects. Center point runs were randomized
105 with a 2-block distribution (10 random runs with 3 center point replicates for each block). A
106 blocking variable was included to reduce the impact of possible nuisance variables throughout
107 the experimentation period (2 month) (Montgomery, 2013). **Table 1** shows all the
108 experiments in the standard and real order of runs with coded and experimental values of the
109 factors.

110 ***2.2. Wines***

111 All experimental distillations were carried out at the Departament d'Enginyeria
112 Química of the Universitat Rovira i Virgili. The CCD distillations used a *Vitis vinifera*
113 "Muscat" wine (2015 vintage year), with an alcoholic strength by volume of 12.6 % (v/v) and
114 a pH of 3.20, which was donated by Dalmau Hermanos y Cía. Suc. S.A. (Tarragona, Spain).
115 The pH of the wine was adjusted before each assay with sulfuric acid solution 2.5 M (GAB
116 system, Barcelona, Spain) at three levels (3.20, 2.45 and 1.70) according to the CCD method
117 (**Table 1**). The pH levels were chosen with the intention of observing marked differences.

118 Optimal distillations used a *Vitis vinifera* "Muscat" (2016 vintage year) with an

alcoholic strength by volume of 11.5 % (v/v) and a pH of 3.20, as well as a *Vitis vinifera* "Macabeo" (2016 vintage year) with an alcoholic strength by volume of 10.6 % (v/v) and a pH of 2.95. Both wines were donated by Cooperativa de Vila-rodona (Vila-rodona, Tarragona, Spain). Their alcoholic strengths by volume were adjusted to 12.6 % (v/v) with food grade ethanol of 95 % (v/v) (Droguería Boter SL, Badalona, Spain). According to the optimal conditions obtained with the study of Muscat wine (2015 vintage year), the wines' pH levels were adjusted before each assay with a sulfuric acid solution 2.5 M (GAB system, Barcelona, Spain) or sodium hydroxide solution 2.5 M (Sigma-Aldrich; Saint Louis, USA).

2.3. Distillation System

The distillation system (**Figure 1**) was scaled down from a 50 L pilot scale batch packed column (García-Llobodanin et al., 2011) to a 1.5 L glass laboratory scale. A Florence flask (2 L) was coupled to a packed glass column (filled with a 1.1 g copper mesh) and a glass tubular heat exchanger (partial condenser). Both inner heat tubes had 8 mm of internal diameter and 80 mm of length. The system was isolated and introduced in a fume hood at constant recirculating air. The internal reflux was modified by changing the cooling water flow rate (at 20 ºC) of the partial condenser with a peristaltic pump (313S, Watson-Marlow Ltd., Falmouth, England). The boiler was heated with a heating mantle (Fibroman-C 1000 mL, JP Selecta S.A., Abrera, Spain). Distillate samples were collected in 20 mL test tubes. Test tubes were covered with perforated caps to minimize evaporation loss of the most volatile compounds. In addition, the system was equipped with four temperature sensors: two in the partial condenser system (shell outlet, T3; and shell inlet, T4), one after the partial condenser (outlet stream of the inner tube, T2) and half a meter away from the device (fume hood's room temperature, T1). Before the experiments, the peristaltic pump of the partial condenser was calibrated between 0 and 300 mL/min.

2.4. Distillation Process

The 1.5 L of wine was placed in the Florence flask with 3 g of pumice stone. The electrical heating mantle operated at a constant power of 410 W during the first 33 min. Then power was reduced and kept constant at 205 W until the end of each assay. Power values were calculated without considering heat loss. Afterwards, to ensure reproducibility of the first fraction, 300 mL/min of CFR was kept constant during 7 min to achieve total reflux. Power and time values were defined after preliminary experiments (data not shown). Then, 40 min (33 + 7 min) after the onset of the process, CFR was decreased to 100, 65 or 30 mL/min during a HDV of 20, 12.5 or 5 mL according to the experimental design (**Table 1**). After the first sample (S1), the partial condenser was stopped and emptied (CFR = 0 mL/min). The next 13 samples (S2-S14) of 20 mL each were distilled without CFR. The last sample (S14) had an alcoholic strength by volume around 39 % (v/v). Optimal distillations were performed with CFR and HDV values according to the optimal conditions obtained with the Muscat wine (2015 vintage year).

2.5. Chemical Analysis of Wine and Distilled Fractions.

Wine ethanol content was determined by ebulliometry (electronic ebulliometer, GAB instruments, Moja-Olèrdola, Spain), wine pH by a pH-meter (Crison Basic 20, L'Hospitalet de Llobregat, Spain) and ethanol content of all distillation samples (S1-S14) by an electronic density meter (Anton Paar DSA 5000M, Graz, Austria). Distilled samples were grouped in four fractions: head-cut (S1), heart-1 (S2-S7), heart-2 (S8-S13) and tail-cut (S14). A 50 µL of the internal standard solution (400 mg/L of 2-octanol, Sigma-Aldrich, Saint Louis, USA) were added to 1 mL of each fraction (previously adjusted to an alcoholic strength by volume of 40 % v/v). All analyses were performed 21 days after each distillation.

2.6. Chromatographic Analysis

Chromatographic analyses were performed by using a gas chromatograph equipped with a flame ionization detector (GC-FID) (Agilent 6890, Agilent Technologies, Waldbron,

Germany), an autosampler (Agilent 7683, Agilent Technologies, Waldbron, Germany) and a capillary polar column (MetaWAX, 60 of length, 0.25 mm ID and 0.5 µm of phase thickness) from Teknokroma (Barcelona, Spain). Injection (2 µL) was done in split mode (1:5). Injector and detector temperatures were at 250 ºC and 260 ºC, respectively. Oven temperature program was: 40 ºC (5 min), 7 ºC/min up to 100 ºC (15 min), 3 ºC/min up to 140 ºC and 2 ºC/min up to 200 ºC (5 min). Column-head flow was initially set at 0.5 mL/min (28 min) and increased with a rate of 5 mL/min^2 up to 1.1 mL/min (67 min) using helium as carrier gas. Quantifications were carried out by interpolation into calibrations built with a synthetic hydro-alcoholic solution (40 % v/v of ethanol) doped with all compounds at different levels. Reagents' CAS, supplier companies and Kovats retention indices are shown in **Table S1**. Detection and quantification limits were determined by Signal-to-Noise ratios (S/N) of 3 and 10, respectively.

2.7. Response Surface Methodology (RSM)

RSM aims to screen, model and optimize an experimental design by studying the relationships between two or more independent variables (factors) and a response (compound concentration). In addition to factors of CCD (HDV, pH and CFR of **Table 1**), the volume of the heart-cut fraction was added to the model as a fourth factor. For that, the composition of heart-1 (120 mL) plus a percentage of heart-2 (0 to 100 % of 120 mL) was considered as a model response. The 0, 50 and 100 % of heart-2 (HTV) were the three levels chosen for the RSM. It should be noted that the response variation produced by HTV is not necessarily linear, since the concentration of the compounds (g/hL a.a.) depends on the alcoholic content of both fractions (% v/v). In this way, the relative impact of distillation sub-fractions could be evaluated. Therefore, after the CCD was performed, a 3-level-4-factor RSM could estimate a second-degree polynomial model with all the compiled data.

2.7.1. Response Surface Models

In this study, sum-of-squares type III was used to calculate the error terms for

statistical significance of linear and quadratic main factor effects and the 2-way interaction factor effects (Montgomery, 2013). Non-significant effects ($p > 0.05$) were ignored to obtain more accurate estimation models. The RSM estimated response for each compound was calculated using the following second-degree polynomial function with four factors:

$$\hat{Y} = b_0 + block1 + b_1 \cdot HTV + b_2 \cdot HDV + b_3 \cdot pH + b_4 \cdot CFR + b_{1,1} \cdot HTV^2 + b_{2,2} \cdot HDV^2 \; b_{3,3} \cdot pH^2 + b_{4,4} \cdot CFR^2 + b_{1,2} \cdot HTV \cdot HDV + b_{1,3} \cdot HTV \cdot pH + b_{1,4} \cdot HTV \cdot CFR + b_{2,3} \cdot HDV \cdot pH + b_{2,4} \cdot HDV \cdot CFR + b_{3,4} \cdot pH \cdot CFR \quad \textbf{(eq.1)}$$

Where $\hat{Y}$ is the estimated response for each compound (concentration in heart-Cut fraction). *HTV*, *HDV*, *pH* and *CRF* are the coded factor values (±1). *block1* is the blocking variable; $b_{i,j}$ are regression coefficients whose subscripts stand for: 0 is the interception of the function, 1 is the HTV, 2 is the HDV, 3 is the pH and 4 is the CFR.

As it has been introduced in **section 2.1**, adding a blocking variable to the model allows us to minimize the effect of a known nuisance variable by arranging the experimental runs in similar groups. In our case, we separate the experiments in two groups (blocks) according to their order of execution. In sum, blocking modifies the origin of the coordinates of a group of samples to minimize a nuisance variation, allowing a better fit of the relevant variables of the study. In this study, experiments 1 to 10 were used to determine b_0 + *block1*, while experiments 11 to 20 were used to determine b_0.

Therefore 40 experimental points were extracted from the 20 experimental assays, because for every assay 2 heart fractions were analyzed (heart-1 and heart-2), specifically 30 data points (without counting central point replicates) and 16 regression constants (counting the blocking variable).

For compounds with low levels, concentration values below the detection limit were considered as 0 g/hL a.a., and values between detection and quantification limits were considered as the average of both limits.

2.7.2. Desirability function approach

Multi-objective optimization aims to calculate one optimal solution that groups several objectives simultaneously. Derringer & Suich (1980) suggested transforming the estimated responses (RSM) into a range of acceptability values between 0 (undesirable) and 1 (very desirable). For optimizing, desirability functions are based on three response types: Nominal-The-Best (NTB-type) to obtain a target value, Larger-The-Best (LTB-type) to maximize the response, and Smaller-The-Best (STB-type) to minimize the response. A more detailed mathematical explanation can be found in Costa, Lourenço & Pereira (2011).

Starting from the assumption that each compound has a positive or negative aroma effect, LTB- and STB-type functions were used in this study. Curvature between inflection points of the function was not considered. In order to transform the estimated response to a linear desirability function, the following concentration points were used for each compound:

- Lower limit point: the compound odor threshold, assigned to a desirability value of 0 (for the LTB-type) or 1 (for the STB-type). This limit was selected since it makes no sense to do an organoleptic optimization of a compound below the consumer perception.
- Upper limit point: the maximum concentration analyzed in all CCD assays, assigned to a desirability value of 1 (for the LTB-type) or 0 (for the STB-type).

Therefore, the individual desirability of each compound increased (LTB-type) or decreased (STB-type) proportionally to the concentration range above the odor threshold, to maximize or minimize the response according to its positive or negative odor effect on the spirit, respectively. **Figure S1** (supplementary information) shows a graphical example of the implementation of the desirability function in this study. Odor description, desirability function-type, odor thresholds and maximum concentration for each compound are shown in **Table 2**.

To group several individual functions in a single multi-objective solution, Derringer & Suich (1980) suggested obtaining an overall desirability by calculating the geometric mean of the individual desirability of the compounds involved in each optimization. Thus,

optimization aims to find the values of the factors that maximize an overall desirability.

2.8. Sensory Analysis

Sensory analysis was performed in the tasting room of the Facultat d'Enologia of Universitat Rovira i Virgili in compliance with standard NF V09-105 (AFNOR, 1987). The training period was conducted in 14 sessions of 1 hour each with a selection of 17 assessors. During training sessions, samples of ethyl alcohol of agricultural origin (40 % v/v) (Alcohol Suave, Bodegas y Destilerías Lehman S.A., Tortosa, Spain) were spiked at several levels of ethyl acetate as a Glue-like descriptor (0 to 300 mg/L range), linalool as a Terpenic descriptor (0 to 12 mg/L range) and ethyl hexanoate as a Fruity descriptor (0 to 4 mg/L range). Moreover, assessors were taught to differentiate spirits fractions by identifying the Tail-like descriptor using tail cut fractions from spirit samples of a previous research (Matias-Guiu et al., 2016) diluted at several levels.

For the sensory characterization of optimal distillation strategies (3 Muscat and 3 Macabeo), assessors scored samples using 4 aroma attributes (Terpenic, Fruity, Glue-like and Tail-like) and a hedonic test, both using 11-point scales from 0 to 10. Two sessions were held to replicate the analysis for each assessor, using Latin square designs (Montgomery, 2013). During the first 10 minutes of both sessions, assessors analyzed the optimizations produced with the Muscat 2016 wine. Then, after 10 minutes of rest, Macabeo 2016 wine optimizations were analyzed during another 10 minutes. For data analysis, the Product Characterization tool of XLSTAT-Sensory statistical package was applied to check if the scores given by the judges were significantly different (ANOVA model: Score = product effect + judge effect + session effect). In both training and analysis, 5 mL of samples were served in black glass cups and assessors had access to drinking water.

2.9. Statistical Analysis

The CCD, RSM and the Desirability Function Approach were performed with

STATISTICA 7.0 statistical package. ANOVA, Tukey's HSD test ($p < 0.05$), Spearman correlation test, Principal Component Analysis (PCA) and Product Characterization (a XLSTAT-Sensory tool) were performed with XLSTAT 2017 statistical add-in for Microsoft Office.

3. Results and Discussion

3.1. Center Point Analyses

3.1.1. Volatile composition of Head and Heart Fractions

Center point (six replicates) was applied to analyze the distillation kinetics of volatile compounds and their variance. **Table 2** presents the studied compounds (18 quantified compounds out of 20 calibrated, showed in **Table S1**) grouped according to their distillation behavior and physical-chemical characteristics (Cortés, Gil, & Fernández, 2009; Jouret et al., 1998; Matias-Guiu et al., 2016). For all the studied compounds, the table includes their odor descriptors, odor desirability function-type, odor thresholds, maximum levels found in all assays of CCD and their concentration through the distillation of the center point.

In the center point, compositions of all compounds showed significant differences at least between two fractions. Head compounds group (acetaldehyde, acetal and ethyl acetate (C_2)) and fruity esters group (ethyl butyrate (C_4), ethyl hexanoate (C_6), ethyl octanoate (C_8) and ethyl decanoate (C_{10})) were mostly distilled during the head-cut due to their high vapor pressure and/or high solubility in ethanol. In spirits distillations, the head-cut is implemented to reduce the content of negative impact aromas (such as of acetaldehyde and ethyl acetate) and toxic compounds (such as methanol) in the product (Christoph & Bauer-Christoph, 2007). The C_4-C_{10} ethyl esters are known for their high positive impact on spirits aroma, having low odor thresholds and providing fruity notes (Christoph & Bauer-Christoph, 2007). Even though methanol showed higher concentrations in the head-cut than in heart-1, it is not considered to be a head compound, since it presented high levels in both the first and the last distillation

297 fractions (Carvallo, Labbe, Pérez-Correa, Zaror, & Wisniak, 2011) and its acceptance level
298 depends on its legal regulation (European Commission, 2008) rather than its aroma impact.
299 Acetic acid also showed high concentrations in the head-cut due to its formation by the
300 hydrolysis of ethyl acetate (Christoph & Bauer-Christoph, 2007), despite its high boiling point
301 (118 ºC) (Environmental Protection Agency, 2012) and high water solubility (K_{OW} = -0.17).
302 Although, in the heart-cut it presented significantly lower values than its threshold.

303 The higher alcohols group (1-propanol, 1-hexanol, 2-methyl-1-butanol and 3-methyl-
304 1-butanol) and the terpenic compounds group (linalool and α-terpineol) tended to distill
305 during heart-1, due to their higher boiling point and/or solubility in water with respect to head
306 and fruity ester compounds groups. At high levels, higher alcohols are known for their
307 negative impact on the spirit's aroma (fusel-like flavors). In turn, terpenic compounds are
308 known for their high positive impact, providing the typical flowery notes from Muscat wines
309 (Christoph & Bauer-Christoph, 2007). In our distillates, some of the compounds of both
310 groups, like 1-propanol and α-terpineol, showed much lower concentrations than their odor
311 thresholds (**Table 2**).

312 Tail compounds (furfural, ethyl lactate and β-phenylethanol) distilled mainly in the
313 last fraction (heart-2), given their high boiling points and/or water solubilities. Tail
314 compounds are considered a defect in young wine spirits, especially furfural compounds that
315 give burned and sweet aroma notes. However, they can add positive characteristics to other
316 type of spirits, e.g. β-phenylethanol may provide a positive rose flavor and furfural may
317 contribute to toasted wood aroma (Christoph & Bauer-Christoph, 2007).

318 Methanol, recognized as a toxic compound, presented much lower concentrations than
319 the legal limit of 200 g/hL a.a. for wine spirits in all collected fractions (European
320 Commission, 2008). In addition, ethyl carbamate, a carcinogen compound of Group 2A
321 according to the International Agency for Research on Cancer (IARC Working Group on the
322 Evaluation of Carcinogenic Risks to Humans, 2010), was not detected in any fraction with an

analytical detection threshold of 0.2 mg/L (40 % alc. v/v).

3.1.2. System Variance

Traditionally, in the spirits industry, distillation columns do not operate at adiabatic conditions and this hinders the production of distillates with consistent composition. In this study, heat insulation significantly improved the experimental reproducibility of the distillation runs. However, it was difficult to completely avoid or control external variables with this distillation system (García-Llobodanin et al., 2011). The relative standard deviations calculated from data of **Table 2** for head-cut were high, especially for ethyl lactate (28 %), ethyl octanoate (38 %), ethyl butyrate (40 %) and ethyl hexanoate (44 %). Nevertheless, relative standard deviations in the compositions of the fractions that give rise to the product (heart-1 and heart-2) were below 12 % in all compounds. The effect of room temperature and distillation time on the composition of center point replicates was checked by simple regression with no significant differences ($p < 0.05$) (data not shown).

3.2. Response Surface Analysis

Linear, quadratic and 2-way interaction regression coefficients, as well as adjusted correlation coefficients of the model for the rescaled factors (**eq. 1**), are shown in **Table 3**. In supplementary information, **Table S2** shows other statistical parameters to measure the goodness of fit of the models and **Figure S2** presents contour plot examples that can help the interpretation of the models, explained by regression coefficients of **Table 3**.

Some compounds presented a statistically significant lack of fit F-test ($p < 0.05$) due to their low concentrations in heart-2 (C_4-C_6-C_8-C_{10} ethyl esters) and heart-1 (β-phenylethanol) fractions (**Table S2**). This can be explained because when the concentrations of the replicates are around quantification limit, a large deviation is produced between analytical values above the limit and those below; when the concentrations of all replicates are below the quantification limit, replicates have identical or very similar concentration values, which imply a pure error that tends towards zero. In both situations, the lack of fit F-test may be

significant. Therefore, in these cases, the goodness of fit is analyzed by the analysis of variance of sums of squares (< 0.0001 for all models) and the adjusted correlation coefficient.

Blocking coefficients were significant in almost all models. Most volatile compounds presented positive blocking coefficients (acetal and C_2-C_4-C_6-C_8 ethyl esters) except for acetaldehyde. The remaining compounds had a negative coefficient, except for acetic acid, which was in equilibrium with ethyl acetate. Thus, the system's rectification could change through the days of experimentation by an unknown external factor that we could not control. In supplementary information, **Figure S2** shows counter plot examples that can help the interpretation of the models explained by regression coefficients of **Table 3**.

To clear up the following discussion of the effects of the studied factors on distillation time during the head-cut, Tukey's (HSD) test pairwise comparisons after a multi-way ANOVA ($p < 0.05$) were performed with head-cut distillation time (dependent variable) and pH, CFR and HDV factors (explanatory variables). Significant differences were found between 30 and 100 mL/min CFR levels and between all HDV levels. The pH showed no significant effects. Thus, higher CFR (higher reflux) and higher HDV (larger head-cut volume) increased distillation time (data not shown).

3.2.1. Distillation-cuts (HTV and HDV) Factors

As can be seen in **Table 3**, HTV and HDV linear regression coefficients of each compound presented identical signs (+ or -) as long as both effects were significant, since both factors depend on distillation kinetics previously explained in **section 3.1.1.**

Ethanol, head compounds, fruity ethyl esters and linalool tend to distill in higher concentrations at the beginning of the distillation (Matias-Guiu et al., 2016). Hence, larger HDV increased their extraction during the head-cut and consequently reduced their levels in the heart-cut. In addition, since the concentration of these compounds in the boiler is significantly reduced during the last fractions, a larger HTV dilutes them in the heart cut. Consequently, both factors present negative linear coefficients. On the contrary, tail

compounds and α-terpineol tend to form and distill in later fractions of the process. Thus, larger HDV increased their concentrations in the heart-cut because there is a displacement of the tail cut, since heart-cut keeps the recovered volume, as well as an increase of the distillation time. Likewise, larger HTV increased tail compounds levels in the heart-cut by adding last distillation fractions. Therefore, both factors presented positive linear coefficients. Higher alcohols and methanol presented no significant effects by HDV. The HTV negatively affects the concentration of higher alcohols by dilution and depletion over time in the boiler (Matias-Guiu et al., 2016) while methanol concentration is positively affected since its relative concentration (g/hL a.a.) increases in the last fractions (Carvallo et al., 2011).

3.2.2. pH Factor

The distillation of wine occurs in an acidic hot environment with pH between 2.8 and 4.0 (Ribéreau-Gayon, Glories, Maujean, & Dubourdieu, 2006), and temperatures ranging between 78 and 100 ºC. This medium favors the formation or reaction of many volatile compounds present in wine. Therefore, the pH of the raw material can be an essential factor for plan distillation strategies, which, in turn, can be easily modified by the producer.

Table 3 shows that all head compounds presented linear effects by pH, with a positive regression coefficient for acetaldehyde and negative coefficients for acetal and ethyl acetate. In acidic media, acetaldehyde and ethanol react to form acetal (Kłosowski & Czupryński, 2006). Furthermore, ethyl acetate is formed by acetic acid esterification, catalyzed in acid media. Therefore, low pH accelerated the formation of ethyl acetate in the boiler (wine) and increased its concentration in the vapor phase (product) since it is much more volatile than acetic acid. Acetal and ethyl acetate also presented positive quadratic effects with pH, showing lower levels in the 2.45 – 3.20 pH range. Hence, low pH favored acetal and ethyl acetate concentration in the heart-cut and decreased acetaldehyde concentration.

In the case of fruity esters, their values were below their quantification limits in the last fractions, due to depletion over time. For this reason, the sum of squares regression did

401 not find linear significant differences with pH, given the small variation of their concentration
402 in heart-2. Nevertheless, variations due to pH can be explained with 2-way interaction effects.
403 Fruity esters showed a positive coefficient of HTV-pH interaction for ethyl octanoate,
404 positive coefficients of pH-CFR interaction for all fruity esters, and negative coefficients of
405 HDV-pH interaction for ethyl butyrate and ethyl decanoate. Low pH could favor the
406 formation of fruity esters from their carboxylic acids, as happened with ethyl acetate – acetic
407 acid equilibrium, thus low pH favors removing fruity esters in the boiler due to their
408 formation at the beginning of distillation. Running out of these esters due to pH interaction
409 effects is more noticeable with high values of HTV and CFR (longer esterification time). On
410 the contrary, fruity esters exhaustion is reduced when the head-cut volume is small, since
411 there is a much shorter time for esterification (negative HDV-pH interaction coefficients).
412 Therefore, low pH accelerates the formation of fruity esters by esterification, behavior that
413 would decrease their levels in the spirit if the head-cut volume is too large.

414 In relation to tail compounds, ethyl lactate had a negative linear effect with pH, like
415 ethyl acetate. Even though pH should favor the generation of furfural during distillation due
416 to Maillard reactions (Mottram, 2007; Peña y Lillo, Agosin, Belancic, & Latrille, 2005;
417 Yemiş & Mazza, 2012), this effect was not significant.

418 Linalool and α-terpineol presented positive and negative linear effects with pH,
419 respectively, since linalool and other terpenic compounds tend to transform to α-terpineol in
420 catalyzed hot acid media (Baxter et al., 1978; Bedoukian, 1986; Ohta et al., 1991; Osorio et
421 al., 2004). Terpenic compounds also presented positive quadratic effects with pH, showing
422 lower levels in the 1.70 – 2.45 pH range. In the case of higher alcohols and ethanol, they
423 presented positive effects with pH, probably due to their reaction by esterification at low pH.

424 *3.2.3. Cooling Flow Rate (CFR) Factor*

425 Previous work had shown that high internal refluxes during the heart-cut can
426 significantly alter the distillation behavior throughout the distillation (Matias-Guiu et al.,

2016). The present study focused on head-cut reflux strategies; hence, CFR was applied during the head-cut fraction only and in a narrow flow range to avoid masking the effects of other factors.

Head compounds were efficiently removed during the head-cut with high CFR values, due to their high volatilities and high solubilities in ethanol (Rodríguez-Bencomo et al., 2016), and therefore showed negative linear effects with CFR.

Ethyl hexanoate showed a positive linear effect with CFR, indicating that high rectification held up its distillation during the head-cut, favoring its recovering in the heart-cut (Matias-Guiu et al., 2016). The C_4-C_8 fruity esters also showed pH-CFR and HDV-CFR interaction effects. Positive pH-CFR coefficients indicate that high rectification avoids C_4-C_8 fruity esters distillation during the head-cut and slows down their formation by esterification (at high pH). Negative HDV-CFR coefficients indicate that both factors slowed down the distillation process and, consequently, increased the time for the esterification reaction during the head-cut. Ethyl decanoate (C_{10}) presented the opposite effects with CFR and pH-CFR coefficients, although its correlation coefficient was the lowest observed (Radj = 0.546), therefore analysis of these results should be done with care.

Linalool showed a negative linear effect with CFR, but a positive pH-CFR interaction. High rectification increases the distillation time and therefore the degradation of linalool. However, this effect diminished with high pH since it slows down the reaction (Baxter et al., 1978; Bedoukian, 1986; Ohta et al., 1991; Osorio et al., 2004).

Higher alcohols and methanol presented a negative effect with CFR, except for 2-methyl-1-butanol, indicating that high refluxes during the head-cut favored their recovery in the heart-cut. Tail compounds were not affected by CFR, and acetic acid had the same behavior as its ester form (ethyl acetate).

3.3. Multi-Objective Optimizations

Desirability individual functions were constructed according to odor desirability, odor

453 threshold and the maximum levels found during the experimental distillations (**Table 2**). To
454 compute specific overall desirability functions, only compounds with a maximum
455 concentration above their aroma threshold were considered. Three optimizations were
456 calculated to obtain specific products with defined organoleptic characteristics: head off-
457 flavors reduction (acetaldehyde and ethyl acetate STB-type), terpenic enhance (linalool LTB-
458 type + acetaldehyde and ethyl acetate STB-type) and fruity ester enhance (C_4-C_8 esters LTB-
459 type + acetaldehyde and ethyl acetate STB-type). Acetaldehyde and ethyl acetate were
460 included in all optimizations to minimize organoleptic defects. Ethyl decanoate (C_{10}) was not
461 included in fruity ester enhance since it presented a considerably low fitting correlation
462 coefficient (Radj. = 0.546). Results of the calculated optimal distillation conditions are shown
463 at the top of **Table 4.**

464 *3.3.1. Head Off-Flavors Reduction (HOR)*

465 This strategy should reduce the acetaldehyde and ethyl acetate contents in the heart-
466 cut. The largest HTV (240 mL) should dilute these compounds in the heart-cut, the largest
467 HDV (20 mL) should favor their recovery in the head-cut, the lowest pH (1.70) should
468 enhance acetaldehyde degradation, and the highest CFR (100 mL/min) should concentrate
469 these compounds in the head-cut.

470 *3.3.2. Terpenic Enhance (TEN)*

471 This strategy should significantly increase the content of linalool in the heart-cut.
472 Linalool is the only terpenic compound that showed concentrations above its aroma threshold
473 (**Table 2**) and the most important for Muscat spirits (Agosin, Belancic, Ibacache, Baumes, &
474 Bordeu, 2000; Cacho, Moncayo, Palma, Ferreira, & Culleré, 2013). Low HTV (16.7 %)
475 should concentrate linalool in the heart-cut, the largest HDV (20 mL) should clean the heart-
476 cut from acetaldehyde and ethyl acetate, the highest pH (3.20) should reduce linalool
477 degradation, and the highest CFR (100 mL/min) should reduce linalool loss in the head-cut.

478 *3.3.3. Fruity Esters Enhance (FEN)*

This strategy included operating conditions that, according to the models, would enhance the fruity esters on the heart-cut. Medium HTV (66.7 %) should balance the reduction of head off-flavors and fruity esters due to dilution, lowest HDV (5 mL) should reduce their loss in the head-cut, high pH (2.95) should reduce fruity ester esterification, and highest CFR (100 mL/min) would reduce losses of fruity esters during distillation of the head-cut.

3.4. Evaluation of Optimal Strategies

Two different wines (Muscat and Macabeo of 2016 vintage year) were distilled with the three optimal strategies to assess RSM models and to confirm chemical analyses with a sensory panel. The main difference between both wines is that Macabeo wine is known for having no detectable terpenic compounds.

3.4.1. Optimums Chemical Analyses

Table 4 shows the predicted heart-cut composition of Muscat 2015 wine distilled with the calculated optimal conditions (RSM). In addition, this table shows the mean concentration of heart-cut, standard deviation and significant differences of Muscat and Macabeo 2016 wines distilled with the same optimal conditions.

Most of the times, the assessed strategies performed according to what was predicted by the RSM models. Heart-cuts of both wines distilled with the FEN strategy showed in most cases the highest values of C_4-C_{10} ethyl esters. The TEN strategy applied to the Muscat 2016 wine yielded the highest levels of linalool and geraniol in the heart-cut. Geraniol was not taken into account during RSM since Muscat 2015 wine and spirits showed geraniol levels below its quantification limit. Macabeo had no detectable terpenic compounds in both spirits and wine (data not shown). The HOR strategy showed the lowest values of acetaldehyde; however, it also showed the highest values of ethyl acetate and unexpected high values of other ethyl esters. As explained in **section 3.2**, we could infer from the RSM models that ethyl esters increase with low pH; however, RSM models predict a decrease of their concentration

505 with high head-cut and heart-cut volumes, which has not observed in 2016 wine distillates. As
506 can be seen throughout **Table 4**, the rest of the compounds have a similar ratio of
507 concentrations between optimal strategies. Thus, deviation of ethyl esters in head off-flavor
508 reduction can be due to compositional changes of wines. Chemical analyses of the three initial
509 wines were carried out to understand this behavior (data not shown) without consistent
510 conclusions. Furthermore, ethyl esters obtained low p-value in the lack of fit F-test, initially
511 attributed to their low levels in heart-2; therefore, the model may generate a wrong prediction
512 of the ethyl esters composition for the HOR strategy.

513 *3.4.2. Optima Sensory Analysis*

514 Samples of the optimal strategies using both wines (Muscat and Macabeo of vintage
515 2016) were sensory analyzed by 17 trained assessors by rating Terpenic, Fruity, Glue-like and
516 Tail-like aroma descriptors, plus a hedonic rating test.

517 In order to reflect the aroma differentiation between samples, sensory data was
518 analyzed by PCA (**Figure 2**). Two principal components (PC1 and PC2) explained 93.6 % of
519 the variance. Glue-like aroma was not included, as it presented no significant differences ($p <$
520 0.1). The PC1 axis places Fruity and Terpenic aroma descriptors against Tail-like descriptor,
521 and PC2 places Fruity descriptor against Terpenic and Tail-like descriptors. This arrangement
522 in the biplot appears to be related with the compound groups associated to descriptors,
523 explained in **section 3.1.1.** The optimal strategies were well differentiated by PCA. Muscat
524 and Macabeo FEN samples presented high intensity of fruity aroma, and Muscat TEN sample
525 presented high intensity of terpenic aroma. Macabeo TEN sample was located near Macabeo
526 FEN sample, but with less fruity intensity. As expected, Macabeo spirits samples showed no
527 terpenic aroma. Muscat and Macabeo HOR samples presented high intensity of tail-like
528 aroma, since this strategy contained last fractions of the distillation to dilute acetaldehyde and
529 ethyl acetate in the heart-cut.

530 Finally, the preference test was analyzed with ANOVA and then Tukey's HSD test (to

check the acceptance between samples) and with the Spearman correlation test (to check the correlation between aroma attributes and consumers acceptance). Hedonic data analysis can only be taken into account as a suggested trend given the small number of assessors and their previous training. Tukey's pairwise compassions (data not shown) showed significant differences ($p < 0.05$) between the Muscat TEN and FEN samples (highest ratings), and Muscat HOR samples (lowest rating). Macabeo samples showed no significant differences. Hedonic rating correlations ($p < 0.05$) showed that samples with terpenic and fruity aromas were scored positively, and samples with glue-like and tail-like aromas were scored negatively (**Figure S3**). This hedonic results illustrate how developing and implementing distillation strategies can favor the production of genuine beverages that retain or enhance flavors coming from the initial fermented beverage, like terpenes (grape origin) and fruity ethyl esters (alcoholic fermentation origin).

4. Conclusions

High rectifications during distillation of the head-cut resulted in improved spirits, characterized by low content of head compounds and high content of fruity and terpenic compounds. The effect of distillation volumes and pH should be considered and adjusted when different groups of volatile compounds are needed to optimize the results, depending on which aromas should be enhanced or reduced. A larger heart-cut decreased all studied compound levels, except tail compounds (off-flavors), α-terpineol (without odor impact at spirit levels) and methanol (toxic compound). A larger head-cut decreased the concentration of head compounds (off-flavors), at the cost of reducing C_4-C_{10} ethyl esters and linalool levels (positive odors) and increasing the level of tail-cut compounds (longer distillation time). Low pH favored the decomposition of linalool and acetaldehyde to form α-terpineol and acetal, respectively, and favored the formation of ethyl esters by esterification. Sensory analysis corroborated the optimization of aroma compounds in spirits by chemical modeling using RSM. These results reinforce the versatility of this experimental system and deepen its ability

to modify the aroma profile of spirit beverages.

5. Acknowledgments

P. M.-G. appreciates the Ph.D. Grant “Martí Franquès” (2015PMF-PIPF-29) with the support of the Universitat Rovira i Virgili.

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684

Figure Captions

Figure 1. Sketch of the distillation device. T1 to 4 are temperature sensors. Expect for T1, distances and dimensions between device parts were maintained using an original drawing.

Figure 2. PCA biplot of the sensory profile of optimal distillation strategies (HOR, FEN and TEN) using Muscat (Musc.) and Macabeo (Maca.) wines of 2016 vintage and filtering the non-discriminant descriptors ($p < 0.1$).

1 **Tables**

Table 1. Central Composite Design 3-level-3-factor with face centered Axial Points (AP) and 6 Center Points (CP). Uncoded values are shown in brackets.

Run number	Run order	Head-Cut Volume (mL)	Cooling Flow Rate[a] (mL/min)	pH
1	2	-1 (5.00)	-1 (30.0)	-1 (1.70)
2	1	+1 (20.0)	+1 (100)	-1 (1.70)
3	5	+1 (20.0)	-1 (30.0)	+1 (3.20)
4	3	-1 (5.00)	+1 (100)	+1 (3.20)
5	12	+1 (20.0)	-1 (30.0)	-1 (1.70)
6	9	-1 (5.00)	+1 (100)	-1 (1.70)
7	10	-1 (5.00)	-1 (30.0)	+1 (3.20)
8	8	+1 (20.0)	+1 (100)	+1 (3.20)
9 (AP)	13	0 (12.5)	0 (65.0)	-1 (1.70)
10 (AP)	17	0 (12.5)	0 (65.0)	+1 (3.20)
11 (AP)	16	0 (12.5)	-1 (30.0)	0 (2.45)
12 (AP)	15	0 (12.5)	+1 (100)	0 (2.45)
13 (AP)	18	-1 (5.00)	0 (65.0)	0 (2.45)
14 (AP)	19	+1 (20.0)	0 (65.0)	0 (2.45)
15 (CP)	6	0 (12.5)	0 (65.0)	0 (2.45)
16 (CP)	4	0 (12.5)	0 (65.0)	0 (2.45)
17 (CP)	11	0 (12.5)	0 (65.0)	0 (2.45)
18 (CP)	7	0 (12.5)	0 (65.0)	0 (2.45)
19 (CP)	20	0 (12.5)	0 (65.0)	0 (2.45)
20 (CP)	14	0 (12.5)	0 (65.0)	0 (2.45)

[a] Partial condenser cooling was applied during the Head-cut distillation only.

2

3

Table 2. Compounds groups, names, odor description, odor desirability, odor threshold and Heart cut maximum levels throughout CCD, and concentrations, standard deviation and significant differences ($p<0.05$) between distillation fractions of the 6 RSM Center Point replicates) [a].

Compound		Odor description	Odor desirability	Odor threshold	Heart-cut maximum levels of CCD	Fraction concentration		
Group	Name					Head-cut	Heart-1 cut	Heart-2 cut
Alcohol content	Ethanol (% v/v)	Alcoholic	-	-	71.0	87.7±0.4c	70.5±0.5b	55.2±1.4a
Head compounds	Acetaldehyde	Pungent	STB	25.0 [b]	171	839±102c	121±10b	9.68±0.64a
	Acetal	Fruity/Sherry	-	0.250 [b]	38.0	153±25c	25.5±1.7b	2.67±0.29a
	Ethyl acetate	Solvent	STB	12.5 [c]	35.4	227±34b	18.5±1.9a	3.72±0.43a
Fruity esters	Ethyl butyrate	Fruity	LTB	0.005 [b]	0.263	1.95±0.78	d. - n.q.	n.d.
	Ethyl hexanoate	Fruity	LTB	0.0013 [b]	0.956	2.20±0.98b	0.699±0.065a	d. - n.q.
	Ethyl octanoate	Fruity	LTB	0.0005 [b]	1.21	1.13±0.43b	0.980±0.113b	0.090±0.031a
	Ethyl decanoate	Floral/Brandy	LTB	0.105 [d]	0.14	0.520±0.092b	0.117±0.007a	0.087±0.024a
Tail compounds	Ethyl lactate	Lactic	-	25.0 [b]	28.7	0.396±0.112a	10.3±1.2b	35.6±3.6c
	Furfural	Burned	-	5.10 [c]	0.480	n.d.	d. - n.q.	0.600±0.056
	β-phenylethanol	Rose	-	2.50 [b]	2.00	0.149±0.024a	0.763±0.077b	2.62±0.26c
Terpenic compounds	Linalool	Floral/Muscat	LTB	0.250 [e]	2.43	0.197±0.017a	1.72±0.11c	0.576±0.028b
	α-terpineol	Floral	-	75.0 [e]	2.00	0.248±0.022a	1.78±0.18b	1.81±0.14b
Higher alcohols	1-hexanol	Mown grass	-	5.00 [f]	1.29	0.295±0.03a	1.26±0.09b	0.334±0.01a
	1-propanol	Fusel-like	-	208 [b]	51.5	26.3±4.7a	48.8±5.8b	38.1±3.5b
	2-methyl-1-butanol	Fusel-like	-	7.50 [b]	26.4	6.59±1.05a	25.8±2.5b	6.73±0.43a
	3-methyl-1-butanol	Fusel-like	-	7.50 [b]	168	41.9±5.2a	162±16c	55.3±3.8b
Others	Methanol	-	-	167 [b], 200 [g]	92.2	108±18b	75.9±9.2a	99.5±10.6b
	Acetic acid	Vinegar-like	-	50.0 [e]	16.0	247±23b	9.67±0.84a	8.04±0.54a

[a] Except ethanol (% v/v), all compounds are expressed in g/hL a.a. "d. - n.q." means detected in at least one replicate, but not quantified. "n.d." means no detected in any replicate. "-" means there is not enough information. "LTB" means Larger-The-Best. "STB" means Smaller-The-Best.

[b] Referenced in Christoph & Bauer-Christoph (2007). [c] Referenced in Clutton & Evans (1978). [d] Referenced in Pino, Tolle, Gök & Winterhalter (2012). [e] Referenced in Cacho, Moncayo, Palma, Ferreira & Culleré (2012). [f] Referenced in Apostolopoulou, Flouros, Demertzis & Akrida-Demertzi (2005). [g] European legal limit (European Commission, 2008).

4

Table 3. Compounds Heart-cut concentration models. Significant regression coefficients values ($p < 0.05$) with their standard errors of linear (L), quadratic (^2) and 2-way interaction (-) effects by HTV, HDV, pH and CFR rescaled factors (±1), and equation's adjusted correlation coefficient (R-adj) [a].

Compound / Coefficient	Intercept	Block1	HTV (L)	HDV (L)	pH (L)	CFR (L)	HTV(^2)	HDV(^2)	pH(^2)	CFR(^2)	HTV-HDV	HTV-pH	HTV-CFR	HDV-pH	HDV-CFR	pH-CFR	R-adj
Ethanol (% v/v)	65.3 ±0.1*	-0.14 ±0.116	-3.90 ±0.13*	-0.692 ±0.148*	0.190 ±0.148	n.s.	1.30 ±0.22*	n.s.	-0.477 ±0.227*	n.s.	-0.208 ±0.179	n.s.	n.s.	n.s.	n.s.	n.s.	0.986
Acetaldehyde	80.5 ±1.3*	-4.38 ±1.52*	-30.5 ±1.8*	-24.6 ±2.1*	7.86 ±2.08*	-8.78 ±2.08*	11.5 ±3.1*	n.s.	n.s.	n.s.	8.29 ±2.52*	n.s.	2.88 ±2.52	4.35 ±2.33*	n.s.	n.s.	0.972
Acetal	16.8 ±0.5*	0.951 ±0.534*	-7.04 ±0.54*	-5.57 ±0.64*	-1.75 ±0.64*	-1.8 ±0.64*	2.65 ±0.94*	n.s.	3.85 ±1.14*	-1.19 ±1.14	1.93 ±0.77*	n.s.	n.s.	-1.27 ±0.71*	-0.982 ±0.714	n.s.	0.952
Ethyl acetate	13.1 ±0.5*	1.05 ±0.54*	-4.44 ±0.57*	-6.62 ±0.67*	-2.56 ±0.67*	-1.04 ±0.67	1.66 ±0.99	n.s.	2.99 ±1.03*	n.s.	2.54 ±0.81*	n.s.	n.s.	n.s.	-0.938 ±0.748	1.41 ±0.75*	0.933
Ethyl butyrate	0.091 ±0.003*	0.014 ±0.007*	-0.037 ±0.008*	-0.062 ±0.01*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.024 ±0.012*	n.s.	n.s.	-0.017 ±0.011	-0.017 ±0.011	0.017 ±0.011	0.832
Ethyl hexanoate	0.469 ±0.014*	0.062 ±0.016*	-0.155 ±0.017*	-0.159 ±0.02*	n.s.	0.030 ±0.020	0.058 ±0.03*	n.s.	-0.071 ±0.031*	n.s.	0.052 ±0.024*	n.s.	n.s.	n.s.	-0.041 ±0.022*	0.063 ±0.022*	0.930
Ethyl octanoate	0.67 ±0.021*	0.133 ±0.025*	-0.215 ±0.03*	-0.133 ±0.035*	n.s.	n.s.	0.081 ±0.051	n.s.	n.s.	n.s.	n.s.	0.048 ±0.042	n.s.	n.s.	n.s.	0.067 ±0.039	0.871
Ethyl decanoate	0.109 ±0.001*	n.s.	-0.008 ±0.003*	-0.005 ±0.004	n.s.	-0.007 ±0.004*	n.s.	n.s.	n.s.	n.s.	0.005 ±0.004	n.s.	n.s.	-0.005 ±0.004	0.004 ±0.004	0.005 ±0.004	0.546
Ethyl lactate	20.0 ±0.2*	-1.78 ±0.26*	6.66 ±0.31*	1.95 ±0.36*	-1.74 ±0.36*	n.s.	-2.62 ±0.54*	n.s.	n.s.	n.s.	n.s.	-0.958 ±0.441*	n.s.	n.s.	n.s.	n.s.	0.975
Furfural	0.313 ±0.013*	n.s.	0.125 ±0.018*	0.059 ±0.021*	n.s.	n.s.	-0.049 ±0.032	n.s.	n.s.	n.s.	0.033 ±0.026	n.s.	n.s.	n.s.	n.s.	n.s.	0.796
β-phenylethanol	1.49 ±0.01*	-0.133 ±0.017*	0.512 ±0.021*	0.116 ±0.024*	n.s.	n.s.	-0.202 ±0.036*	n.s.	n.s.	n.s.	0.051 ±0.03	-0.032 ±0.03	n.s.	n.s.	n.s.	n.s.	0.979
Linalool	1.3 ±0.02*	-0.055 ±0.019*	-0.321 ±0.021*	-0.071 ±0.024*	0.511 ±0.024*	-0.043 ±0.024*	0.12 ±0.036*	n.s.	-0.077 ±0.037*	n.s.	n.s.	-0.173 ±0.029*	n.s.	n.s.	n.s.	0.029 ±0.027	0.982
α-terpineol	1.82 ±0.01*	-0.145 ±0.017*	n.s.	0.067 ±0.022*	-0.238 ±0.022*	n.s.	n.s.	n.s.	-0.128 ±0.034*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.918
1-hexanol	0.909 ±0.006*	-0.045 ±0.007*	-0.260 ±0.009*	n.s.	0.012 ±0.01	-0.011 ±0.01	0.097 ±0.015*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.985
1-propanol	45.1 ±0.3*	-4.37 ±0.35*	-3.13 ±0.42*	n.s.	0.692 ±0.491	-0.73 ±0.491	1.06 ±0.73	n.s.	n.s.	n.s.	n.s.	-0.706 ±0.595	n.s.	n.s.	n.s.	n.s.	0.938
2-methyl-1-butanol	18.6 ±0.2*	-1.43 ±0.18*	-5.36 ±0.22*	n.s.	0.401 ±0.261	n.s.	2.00 ±0.39*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.978
3-methyl-1-butanol	122 ±1*	-10.0 ±1.1*	-30.1 ±1.4*	n.s.	2.47 ±1.59	-1.91 ±1.59	11.2 ±2.4*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.976
Methanol	85.8 ±0.5*	-8.42 ±0.57*	6.36 ±0.7*	n.s.	n.s.	-1.48 ±0.81*	-2.71 ±1.21*	n.s.	n.s.	n.s.	n.s.	-1.23 ±0.99	n.s.	n.s.	n.s.	n.s.	0.954
Acetic acid	9.49 ±0.18*	0.396 ±0.266	-0.689 ±0.292*	-2.79 ±0.34*	n.s.	-0.786 ±0.341*	n.s.	1.03 ±0.52*	n.s.	n.s.	1.19 ±0.41*	n.s.	n.s.	n.s.	n.s.	n.s.	0.857

[a] Except ethanol, all compounds are expressed in g/hL a.a. HTV means the percentage (%) of Heart-2. HDV means Head-Cut Volume. CFR means Cooling Flow Rate. * $p < 0.001$; n.s. means no significant.

Table 4. Distillation conditions, desirability values and predicted and analytical composition of head off-flavors reduction; terpenic enhance and fruity esters enhance optimums calculated with RSM and desirability function approaches [a].

Distillation conditions	Head off-flavor reduction	Terpenic enhance	Fruity Esters enhance	Head off-flavor reduction	Terpenic enhance	Fruity Esters enhance	Head off-flavor reduction	Terpenic enhance	Fruity Esters enhance
HTV (%)	100	16.7	66.7	100	16.7	66.7	100	16.7	66.7
HDV (mL)	20.0	20.0	5.00	20.0	20.0	5.00	20.0	20.0	5.00
pH	1.70	3.20	2.95	1.70	3.20	2.95	1.70	3.20	2.95
CFR (mL/min)	100	100	100	100	100	100	100	100	100
	Predicted values (RSM) for Muscat 2015 heart cut			*Analytical values for Muscat 2016 heart cut*			*Analytical values for Macabeo 2016 heart cut*		
Desirability value	0.993	0.806	0.658						
Ethanol (% v/v)	61.1	67.6	64.8	56.8 ±0.0 a	62.9 ±0.0 c	61.2 ±0.2 b	56.5 ±0.2 a	63.3 ±0.2 c	61.6 ±0.5 b
Compounds (g/hL a.a.)									
Acetaldehyde	**27.1**	**77.4**	**88.0**	15.5 ±0.3 a	24.9 ±3.1 b	37.1 ±2.6 c	21.5 ±0.6 a	50.5 ±3.2 b	63.7 ±3.8 c
Acetal	11.7	12.7	19.1	8.01 ±0.07 a	9.47 ±0.8 a	17.2 ±1.4 b	10.1 ±0.2 ab	7.38 ±0.01 a	14.2 ±2.7 b
Ethyl acetate	**8.44**	**8.38**	**18.1**	41.9 ±1 c	12.3 ±1.8 a	30.2 ±1.1 b	36.4 ±5.5 c	9.10 ±0.30 a	19.4 ±0.8 b
Ethyl butyrate	0.000	0.022	**0.172**	0.235 ±0.003 a	d.-n.q.	0.296 ±0.005 b	0.218 ±0.046	d.-n.q.	0.256 ±0.005
Ethyl hexanoate	0.119	0.386	**0.648**	1.06 ±0.03 b	0.800 ±0.008 a	1.25 ±0.03 c	0.848 ±0.056 b	0.706 ±0.027 a	1.19 ±0.01 c
Ethyl octanoate	0.287	0.751	**0.795**	1.50 ±0.01	1.53 ±0.06	1.50 ±0.14	1.16 ±0.02 a	1.33 ±0.13 a	1.64 ±0.02 b
Ethyl decanoate	0.097	0.104	0.106	0.319 ±0.054	0.450 ±0.077	0.330 ±0.048	0.203 ±0.037 a	0.252 ±0.013 a	0.338 ±0.014 b
Ethyl lactate	28.7	15.2	18.6	52.2 ±1.8 b	13.4 ±0.5 a	16.4 ±0.1 a	3.90 ±0.15 c	1.12 ±0.14 a	1.84 ±0.26 b
Furfural	0.480	0.244	0.279	d.-n.q.	d.-n.q.	d.-n.q.	d.-n.q.	n.d.	d.-n.q.
β-phenylethanol	2.00	1.17	1.50	3.93 ±0.21 b	2.76 ±0.2 a	3.00 ±0.06 a	2.85 ±0.02 b	1.97 ±0.17 a	2.18 ±0.03 a
Linalool	0.543	**2.03**	1.52	0.128 ±0.003 a	2.17 ±0.14 c	1.62 ±0.03 b	n.d.	n.d.	n.d.
Geraniol	d.-n.q.	d.-n.q.	d.-n.q.	n.d.	0.273 ±0.013 b	0.185 ±0.001 a	n.d.	n.d.	n.d.
α-terpineol	2.00	1.52	1.54	1.01 ±0.06	0.977 ±0.027	0.944 ±0.002	n.d.	n.d.	n.d.
1-hexanol	0.723	1.13	0.831	0.840 ±0.032 a	1.14 ±0.05 b	0.886 ±0.004 a	1.37 ±0.05 a	1.94 ±0.12 b	1.56 ±0.07 a
1-propanol	42.4	48.1	43.8	24.8 ±0.3 a	27.9 ±0.8 b	25.3 ±0.3 a	18.6 ±0.1	21.2 ±1.3	19.2 ±0.6
2-methyl-1-butanol	14.9	23.5	17.3	35.0 ±0.8 a	49.2 ±2 b	38.5 ±0.1 a	19.0 ±0.8 a	27.0 ±1.9 b	21.8 ±0.7 a
3-methyl-1-butanol	99.1	148	113	133 ±2 a	179 ±7 b	142 ±0 a	121 ±4 a	166 ±11 b	135 ±5 a
Methanol	89.2	79.7	85.9	47.9 ±0.8 b	44.2 ±0.6 a	46 ±0.9 ab	44.4 ±0.8	41.8 ±2.4	41.5 ±1.1
Acetic acid	7.46	6.62	11.9	9.98 ±1.18	8.08 ±1.08	10.7 ±0.8	9.17 ±0.61	8.77 ±1.46	11.4 ±0.4

[a] Optimal distillation conditions and desirability values were calculated using the responses in bold. "n.d." means no detected. "d.-n.q." means detected but not quantified.

Figure(s)

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Figure Graphics

Figure 1.

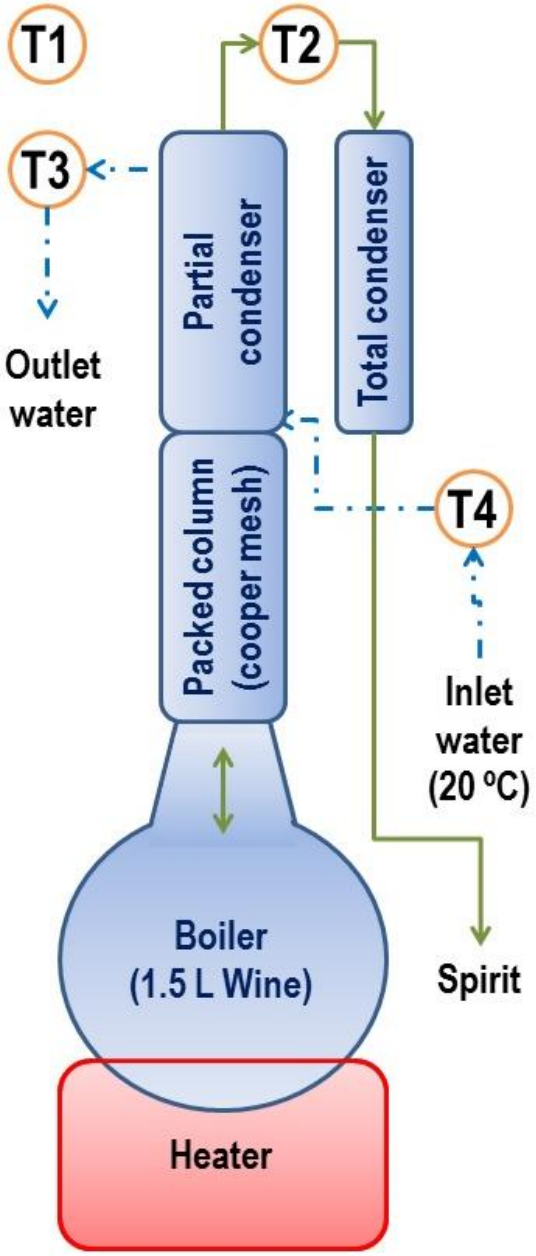
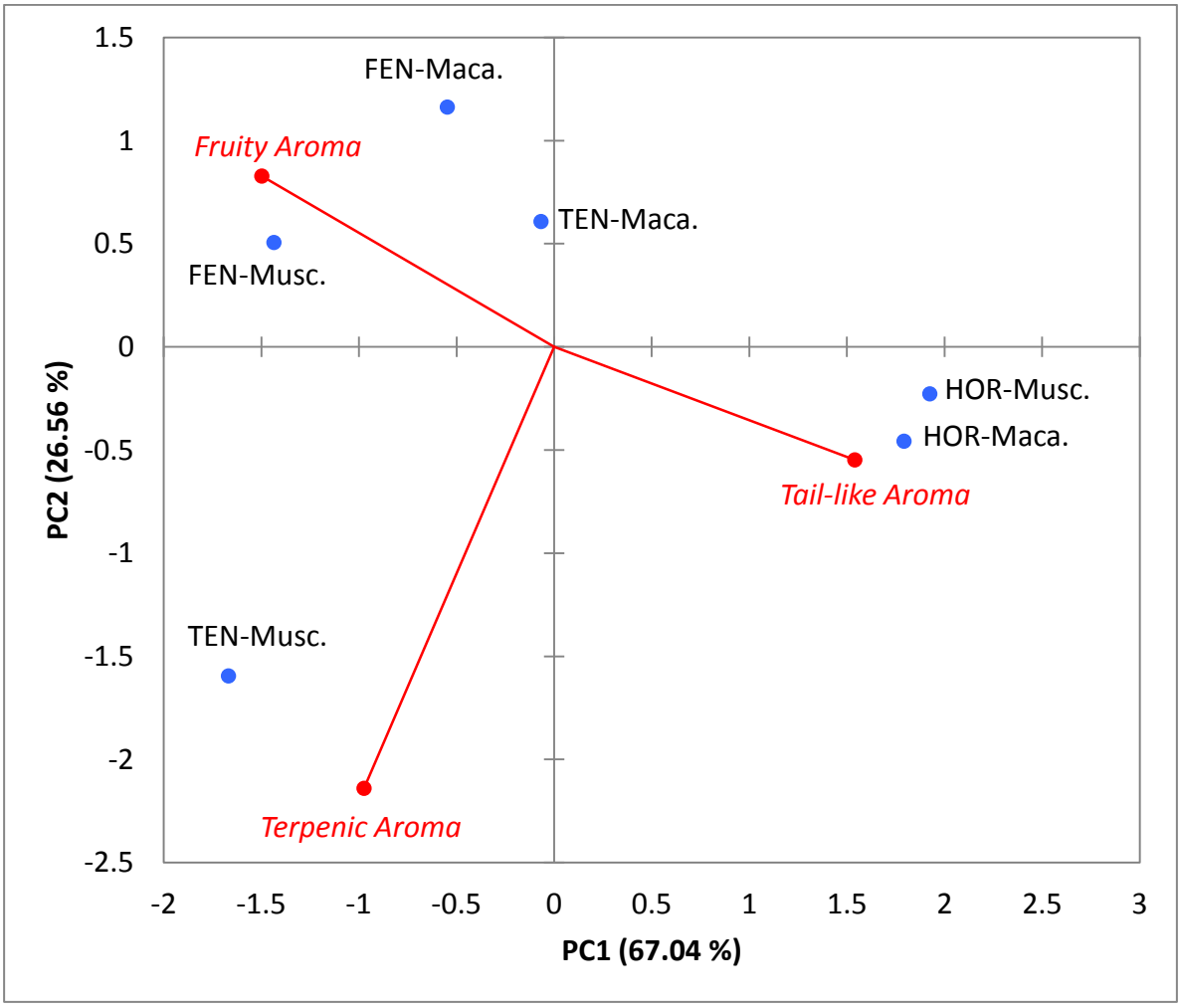


Figure 2.


FEN-Maca.
Fruity Aroma
TEN-Maca.
FEN-Musc.
HOR-Musc.
HOR-Maca.
Tail-like Aroma
TEN-Musc.
Terpenic Aroma
PC2 (26.56 %)
PC1 (67.04 %)
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-2.5
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
2.5
3

Supplementary Material

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