CO_2 - extraction of glycyrrhizic acid from licorice root: optimization of extraction conditions using RSM

Shoxista Mirzayeva[1*], *Laziz* Yuldoshov[1], and *Niyozgul* Xodjiyeva[1]

[1]Bukhara State University, Bukhara, Uzbekistan

Abstract. Extraction of GA (glycyrrhizic acid) from licorice roots was carried out utilizing SC-CO_2 with etilen as a dissolvable. Tests and recreations were assigned utilizing RSM. Licorice root extricate was analyzed by chromatography and AAS. The RSM plan was utilized to optimize the SCE factors and Glycyrrhizic Acid surrender. The most extreme Glycyrrhizic Acid surrender was watched beneath conditions of 10,9 MPa, 90,5 and 49,5 ^{0}C, 93 min and a stream of 1,69 and 1,49 ml/min CO_2 utilizing RSM, separately. Agreeing to RSM, the R^2 and adjusted R^2 model are 95,9% and 92,3% individually. The precision of the GA surrender demonstrate is affirmed by triplet tests, giving an normal extraction abdicate of 51,9 ± 1,19 %, individually, for RSM. ***Key words:*** *Supercritical fluid (*liquid*) extraction, RSM, licorice root, modeling,* the national sweet "nisholla" *optimization.* Designations: P (MPa) – extraction pressure (weight), φ (ml/min) – CO_2 stream rate, R (%) – yield, t (min) – extraction duration (length), E (^{0}C) – processes temperature.

1 Introduction

Liquorice (licorice) is an vital plant that has been utilized since antiquated times in Uzbekistan republic to prepare the national sweet "nisholla". The roots of this plant are wealthy in glycyrrhizic corrosive (GA) (Fig. 1), which includes a sweet taste and is in this manner altogether prevalent to sucrose by 300.

Extraction of Glycyrrhizic Acid can be carried out by steam refining and customary solvents. As of late, from the point of see of natural security, CO_2 in melted and liquid states (SC-CO2) started to be utilized to separate plant fixings, counting Glycyrrhizic Acid from Uzbekistans Licorice [1,2,3].

A few preferences of Supercritical extractions are the high speed of the process, short extraction time and low temperature preventing various chemical changes in Glycyrrhizic Acid, effortlessness and total expulsion of the extricate, and high selectivity of the method, and high selectivity of the process. Hence, Supercritical CO_2 extractions could be a helpful strategy, compared to conventional strategies, CO_2 is the leading extractant of SCE due to moo basic focuses (T = 31,2 ^{0}C, P = 73,9 bar), low extraction temperatures. To move

* Corresponding author: shohista.m@rambler.ru

forward the extraction properties of non-polar CO_2, the polar dissolvable ethanol is included [1].

Fig. 1. Root of Licorice

The reason of this work is to extricate Glycyrrhizic Acid (GA), as the most component of licorice root, using SC-CO_2 with the expansion of ethanol as a modifier utilizing SCF. The contrast between this consider and what is known within the writing lies within the test plan of modeling and optimization of extraction abdicate. The development is the optimization of prepare parameters through RSM, where most extreme yield is accomplished by optimizing extraction conditions. The hypothesized ideal surrender beneath particular conditions is affirmed by triplicate tests (TRI) in this ponder.

2 Experimental part of work

2.1 Material

Liquorice was developed within the test field of the Bukhara Building and Innovation Founded. The dried roots were petaled.

Commercial CO_2 of 99 % purity was used by the Union of CO_2 Extract Manufacturers “Interregional Research and Production Center “Extract Product” for SCE. Standard Glycyrrhizic Acid (GA) (purity ≥95%) obtained from IPS (Tashkent) and standard (purity > 99,9%, Merek) were used for chromatographic analysis

2.2 Supercritical extraction

Supercritical CO_2 extractions was carried out in a research facility setup (Fig. 2).

Depiction of the gadget and working rule of a research facility establishment for CO2 extraction of fixings from plant materials.

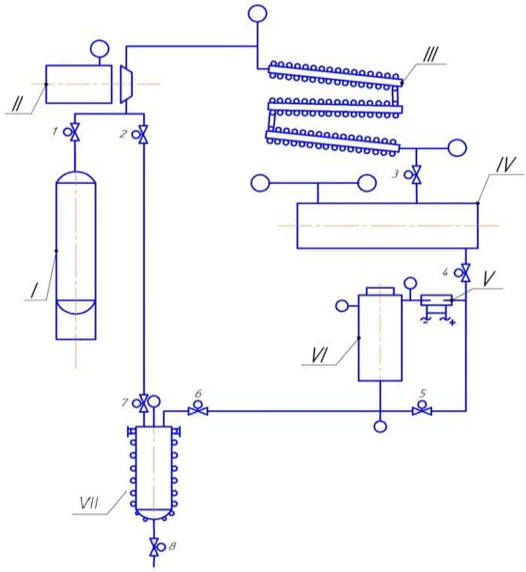


Fig.2. Laboratory installation for CO2 extraction of ingredients from plant materials: I-cylinder with liquefied CO_2; II-compressor; III- capacitor; IV- extractant container; V- heat exchanger; VI-extractor; VII- separator-evaporator.

A research facility establishment for CO_2 extraction of fixings from plant materials works as takes after: pre-crushed plant materials are stacked into a work cassette, which is works in extractor VII. After fixing the extractor, the mechanical framework with the item is cleansed with CO_2 gas to evacuate discuss.

Carbon dioxide from barrel I is exchanged to compressor II with valve 1 open and valve 2 closed (at the primary begin of the establishment). CO_2, compressed by compressor II, passes through condenser IV, where it is cooled by the working operator of the warm pump, turns into a liquid state (P_1=8...10 MPa and T_1=25...30^{0}C) and amasses within the extractant holder V with valve 3 open. In this case, the pressure of the extractant at the entrance to the condenser and its temperature at the exit from the condenser are measured by a weight gage and a TCM thermometer, separately. The weight and level within the holder V are measured by a weight and level sensor, and the signals are transmitted to the control framework to control the operation of valve 3.

To carry out the extraction handle, the fluid solvent, with valve 4 open, passes through the electric radiator VI, where it goes into a supercritical state (P_2=8...10 MPa and T_2=35...70^{0}C) and is provided to the best of the extractor VII, where a temperature sensor is introduced, which sends a signal into an flexible electric radiator framework to control the temperature of the extractant (raw material). The extractant stream rate is directed by valve 4. Having passed through the layer of raw material, the extractant extricates dissolvable components (for example, grape oil) and is evacuated from the lower portion of the extractor, i.e. extraction is carried out by implantation for few time (the settling time depends on the sort of crude fabric being extricated) with valve 5 closed. In the event that the extraction innovation requires flow extraction, at that point the method happens with valve 5 open. coming to the method time, valve 5 closes and throttle valve 6 opens. When passing through this throttle, the pressure and temperature of the miscella diminish underneath critical parameters (P_3 = 5,0...5,5 MPa and T_3 = 25...30^{0}C) and carbon dioxide passes into the vaporous state [2-9].

Within the separator-evaporator IX, precipitation of the extricate broken up within the extractant happens, where it is essential to preserve the temperature (T_4 = 25...30^{0}C).

The temperature is kept up utilizing the working agent of the heat pump, which serves as a thermal agent for the coil radiator of the separator-evaporator. In this case, the accelerated extricate is evacuated from the bottom of the separator-evaporator with valve 8 open, vaporous carbon dioxide is removed from the beat of the separator-evaporator with valve 7 open. Vaporous CO_2 passes through valve 2, is compressed to the operating weight within the compressor and the cycle rehashes.

Within the mechanical conspire, a hot pump to boot associated to cool the extractant in condenser IV and to preserve the desired temperature of the extricate in the theevaporator separator IX. The working agent is compressed in the compressor of the warm pump VIII, passes through the separator-evaporator coil IX, gives up its warm and is cooled, takes off the separator-evaporator coil and passes through the throttle valve III, where it loses weight. The cooled working agent enters the coat of condenser IV, where it takes warm from the extractant, vanishes, and in a vaporous state enters the compressor and the cycle rehashes. Hence, the separator-evaporator coil IX plays the part of the warm pump's condenser, here the working agent, giving up its warm, keeps up the specified temperature to partitioned the extractant from the extricate and condenses, and the condenser shirt IV plays the part of the warm pump's evaporator, where the working agent, taking warm from the extractant dissipates.

2.3 Experiments and measurable information investigation

RSM - design is applied to modeling issues where the reaction (30 v) (subordinate factors) is affected by different components (autonomous factors) through the foundation of numerical and measurable strategies and presumptions of prepare optimization strategies. This strategy requires a few experiments to calculate the parameters and their interactions and is cheap and time devouring compared to other approaches.

In this consider, the experimental design was compiled utilizing CCD (control composite design) with 4 factors: pressure, temperature, CO_2 supply rate and dynamic time in five levels (-2, -1, 0, +1, +2) and $\alpha<2$ Matlab straightforward adaptation. The coded values and the genuine meaning of any code are summarized in table. 1. The boundary surface relapse strategy is utilized in CCD to enter information into a quadratic demonstrate model and decide the number of tests comprising of: 2K test alludes to pivotal focuses at a separate (a) from the center point. For RSM, the number of experiments is 31 for 4 free factors. The exploratory design is completely randomized as indicated, the test center (0, 0, 0, 0) is rehashed seven times. The demonstrated testing experiments and their comes about demonstrating the abdicate (condition (1)) and loss (condition (2)) for GA under various SCE conditions are summarized in table. 2. The volume of expended CO_2 per amount of extricated GA is additionally appeared in this table. Applying multiplet regression experiment to these test information, a second order polynomial condition is the output for BG misfortune (%). P – the esteem of combinations of autonomous factors decides the significance of the relapse coefficient. If the P esteem here is less than the required certainty level, at that point this will be clarified by the reality that the calculate beneath think about is measurably critical. In this think about, factors with $p\leq0{,}001$, $0{,}01<p\leq0{,}01$ and $p>0{,}01$ are considered highly significant, noteworthy and inconsequential, individually, the estimated yield and loss (%) of GA by the RSM model are presented in Table. 2 for comparison. Optimal conditions are obtained for maximum GA extraction yield through RSM prediction. The validity of RSM in modeling optimal GA yield is assessed through triplet experiments.

Table 1. Independent variables and their levels for CCD in RSM design

	Pressure	**Temperature**	**CO_2 flow rate min**	**T, time (min)**
	P	**T**	**Q**	**T**
-2	10,5	50	0,6	5
-1	15,5	60	0,9	7
0	20,5	70	1,4	9
+1	25,5	80	1,8	2
+2	30,5	90	2,2	3

Table 2. Experimental and predicted yields of GA – extraction

№	**D**	**T**	**Q**	**t**	**Yield with supercritical fluid extraction (mg/g)**	**Output from RSM (mg/g)**	**Recovery (%) with supercriti-cal fluid extraction (mg/g)**	**Retrieval (%) with RSM (mg/g)**	**Spent CO_2 in sup. fl. ex. (ml)**	**Extracted GA with supercritical fluid extraction**
1	1	1	−1	1	18,64	20,39	43,95	48,36	92	36,34
2	0	0	0	2	22,65	21,84	53,79	51,89	157	42,27
3	−1	−1	1	−1	15,60	15,95	36,28	37,25	103	28,18
4	−1	−1	1	1	21,89	22,33	51,92	53,12	171	42,76
5	0	0	0	0	20,73	21,21	49,03	51,07	105	38,45
6	1	−1	1	−1	19,53	20,20	46,02	47,95	103	38,10
7	0	0	−2	0	19,78	20,11	46,65	47,73	41	36,52
8	0	0	0	0	22,84	21,00	51,79	51,07	105	40,66
9	0	0	0	−2	13,05	12,54	29,92	28,79	53	24,06
10	0	0	2	0	21,04	22,12	49,79	54,45	169	40,05
11	1	−1	−1	−1	18.85	16,25	46,86	44,56	55	38,69
12	0	0	0	0	22,52	20,50	53,47	51,08	105	44,10
13	0	0	0	0	21,65	21,13	51,32	51,03	105	42,28
14	2	0	0	0	20,24	19,35	47,80	44,89	105	39,45
15	1	1	1	−1	16,52	16,59	39,05	44,49	103	32,41
16	−1	−1	−1	1	19,51	20,32	45,98	49,79	91	37,98
17	−2	0	0	0	10,50	10,10	23,60	23,48	105	19,98
18	−1	−1	−1	−1	14,70	14,19	33,87	33,87	55	28,35
19	−1	1	−1	−1	8,87	8,12	17,05	21,72	55	14,71
20	0	0	0	0	22,09	21,50	52,10	51,09	105	43,15
21	−1	1	1	1	17,89	15,83	41,86	40,95	171	32,75
22	−1	1	1	−1	11,10	10,04	25,19	25,08	103	21,16
23	1	−1	−1	1	20,10	20,79	49,79	51,79	91	38,97
24	0	−2	0	0	22,24	21,41	52,89	53,36	105	43,46
25	1	1	−1	−1	15,22	16,51	37,79	41,13	55	31,41
26	0	0	0	0	20,53	20,51	51,11	51,08	105	42,04
27	1	1	1	1	22,58	20,76	54,23	51,75	171	44,53
28	−1	1	−1	1	14,17	15,09	35,26	37,65	91	29,36
29	0	2	0	0	15,81	15,14	39,38	37,73	105	32,59
30	0	0	0	0	19,54	20,52	48,64	51,09	105	38,04
31	1	−1	1	1	19,35	22,15	48,14	55,13	171	37,68

In order to assess the correctness of the model, an analysis of variables (ANOVA) table is calculated. In this analysis, if the p-value from any source is less than the established confidence level ($p \leq 0.001$), it will be possible to declare that this proposed regression model is statistically significant, i.e. the model is correct. In the same table, the sum of squared errors consists of the sum of losses. The total error depends on the accuracy of the method of determination through repeated experiments. The sum of the absolute error rate should be considered higher than the sum of the loss of sensitivity rate for an appropriate test sensitivity [10–19].

3 Results and discussion

RSM presents a 2nd order polynomial model to explain the variation in GA extraction rate depending on the operating variables. The 2nd order regression coefficients of the model are based on the coded variables and the t and P values corresponding to each code are summarized in Table. 3. Analysis is chip through coded variables. In this analysis, if the P value is less than the specified confidence level, then it can be argued that the factor being studied is statistically significant. Linear terms of temperature, pressure and dynamic time, quadratic terms of dynamic time and pressure with $P \leq 0,001$ are highly reliable. The linear term of CO_2 flux, the quadratic term of temperature and the interaction terms t – p and r - dynamic time with $0,001<p<0,01$ are significant, while the variables with $p>0,01$ are insignificant. By applying multiple regression analysis to experimental data, we can obtain 2nd order polynominal equations (1). The calculated coefficient of determination (R_2) and the selected coefficient (Adj R_2) are respectively equal to 96,64% and 93,22%. These values indicate a good fit of this proposed model, i.e. with experimental data, which is equal to 93,22% of the variables could be covered by the resulting model through equation (1)

$$R=51 \quad (1)$$

Table 3. Regression coefficients of the proposed 2nd order polynomial model for GA.

Start	Coefficient	Extraction coefficient	t-value	D- meaning
Constant	51,044	0,939	54,44	0,000
P	5,354	0,507	10,58	0,000
T	−3,901	0,507	−7,8	0,000
Q	1,676	0,507	3,32	0,005
T	5,774	0,507	11,41	0,000
D× D	−4,223	0,465	−9,11	0,000
T × T	−1,389	0,465	−2,10	0,010
Q × Q **t × t**	−1,093 −2,684	0,465 0,465	−2,36 −5,79	0,014 0,000
T × D	2,195	0,621	3,55	0,004
Q × D	−0,749	0,621	−1,22	0,247
D × t **Q × T**	−2,165 1,399	0,621 0,621	−3,50 2,26	0,004 0,040
T × t	1,612	0,621	1,28	0,020
Q × t	0,784	0,621	1,27	0,226

3.1 RSA

3-D (response surface shape) and 2-D (contour) response surface diagrams are compiled to determine the influence of operating variables on GA extraction. The shape of the response surface is plotted using the response offset (z axis) against two independent variables (x and y coordinates). The other two independent variables are held constant at level 0.

3.1.1 Effect of P and T on GA extraction

In general, P has a dual effect on extraction. Pressure causes volume contraction and increases the density of CO_2. Increasing density reduces the distance between molecules and increases the interaction between solvent and solute molecules. This phenomenon increases the solubility of SK-F during extraction and contributes to the speed of extraction.

Increasing pressure reduces the coefficient of diffusion and mass transfer, so it has a negative effect on the recovery rate. The surface and its type of GA extraction as a function of P and T at a fixed dynamic extraction time (80 min.) and a fixed $SC\text{-}CO_2$ flow rate (1,3 ml/min) is shown in Fig. 3 a, b. As can be seen from the figure, a constant temperature and an increase in pressure of 10 MPa leads to a dynamic effect in increasing density and dissolving force, consequently to an increase in the extraction of GA. Pressure power, reducing diffusion and mass transfer coefficient become more important, increasing pressure reduces GA extraction. As can be seen from table. 4 low pressure values have a positive effect (positive linear effect of pressure ($P \leq 0,001$)) positive effect of T-P interaction (P≤0,01) on % GA recovery. At high pressures, the negative quadratic effect of pressure and the negative interaction effect of P – dynamic GA extraction time will become important factors (P≤0,001 and P≤0,01), respectively. and with increasing pressure the % recovery decreases.

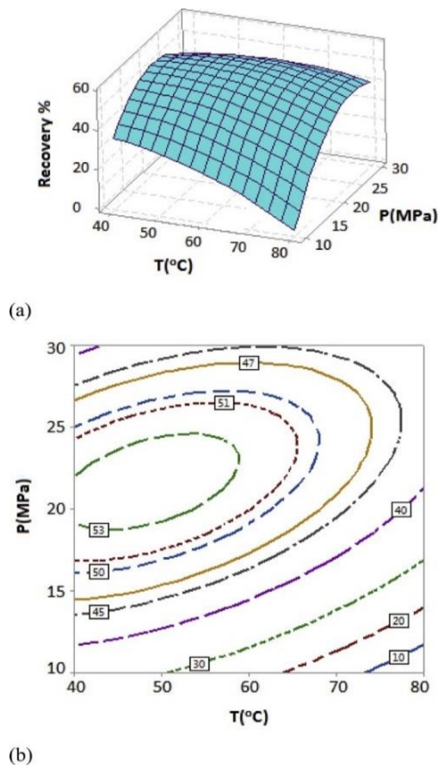


Fig. 3. Response surface (a) and contour view for GA extraction as a function of coded pH and T values at a SC-CO_2 flow rate of 1,3 ml/min and a dynamic time of 80 min.

Increasing T improves the vapor pressure of the solvent, in general therefore it increases the extraction yield to a certain specific state (retrograde solubility). Consequently, a further increase in temperature above retrograde solubility leads to a decrease in the density of SC-CO_2 and a decrease in the solubility of the substance. This effect reduces extraction. This convenient dual effect on the right and left sides of the thermodynamic retrograde phenomenon is evident in the influence of T on the GA extraction yield at pressures higher than the shut-off pressure (code = 04,22 MPa).

According to the dominance of these two convenient effects near the point of retrograde solubility, T could have a different effect on extraction. The phenomenon of retrograde solubility is quite obvious for the dissolution of GA from licorice plant roots.

The phenomenon of intersection is one of the most important for solubility. In fact, different isotherms combine and reverse (invert) the solubility process (behavior). At pressures lower than pressure, the effect of low density becomes greater than the effect of high vapor pressure, so the solubility of the substance (solute) and recovery of the salt decreases, while at pressures higher than crossover pressure, the concept of retrograde temperature appears . As can be seen in Fig. 3, an increase in T from 40^0C to 80^0C leads to a decrease in the extraction yield at pressures not lower than pressure (10 MPa).

In Table 4, P≤0,001 for the linear effect of T confirms this phenomenon. At pressures higher than the pressure, an increase in T at constant P, due to the impact increase in the volatility of the somota, leads to high extraction up to retrograde temperature. This effect occurs due to the positive interaction effect between T and P on % GA yield at a confidence level of P≤0,01. Beyond the retrograde temperature, the effect of low density becomes higher than the effect of high vapor pressure again reducing the solubility and recovery of the salt.

3.1.2 Effect of CO2 molasses rate and dynamic time on GA extraction

Increasing the SC-CO_2 flow rate reduces the film strength around solid particles and increases the film mass transfer coefficient. Stable mass transfer around solid particles and the form of stability is reduced to the transmission of somata through the matrix to the SC fluid and is insignificant, and therefore the increase in the extraction yield of GA. Increasing the CO_2 flow rate reduces the average residual cell extraction time, reduces penetration and leads to poor solid-fluid contact, which leads to reduced GA recovery.

The influence of CO_2 flow rate and dynamic time on the yield of GA at given T (60^0C) and P (10 MPa) is shown in Fig. 4, where increasing the flow rate increases the HA yield at a constant dynamic time. It turned out that the effect of reducing the film strength of the mass transfer layer is higher compared to the reducing effect of residual time. The positive linear effect of SC-CO_2 flow rate (0,001≤ P<0,01) on the responses of the variables is shown in Table. 3.

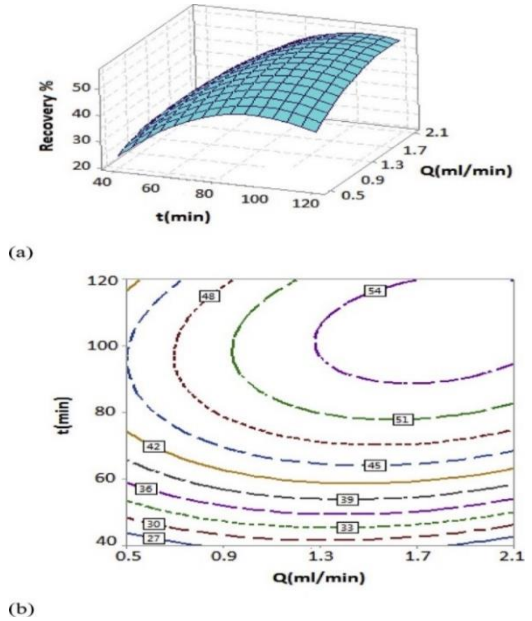
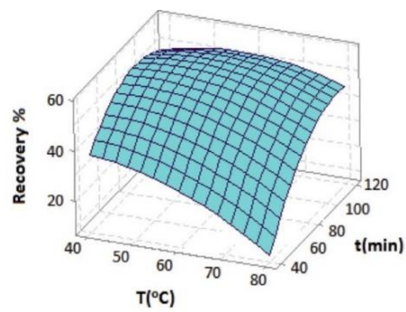


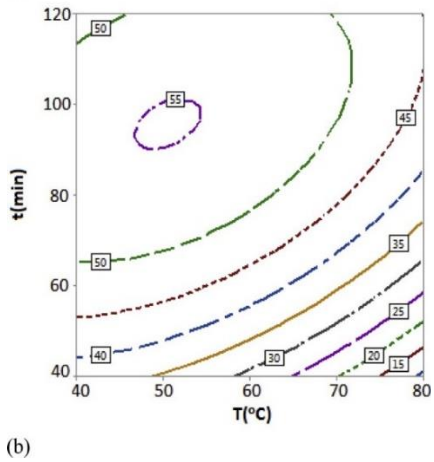
Fig. 4. Response surface and type of contour to the extraction output as a function of the coded values of the CO_2 flow rate (ml/min) and dynamic time (min) at P=10 MPa and T=60^0C.

Over a dynamic period of time, fresh solvent passes through the licorice petals into a fixed vessel. Since the effective mass transfer force exists between the fresh fluid and the sample, increasing the dynamic time improves GA recovery up to the maximum value. Moreover, if the driving force decreases, then high dynamic time is not recommended, so the extraction no longer increases.

The effect of dynamic time and T on the extraction of GA at a fixed flow rate of CO_2 (1,3 ml/min) and P (10 MPa) is shown in Fig. 5, the positive linear effect of dynamic time (P≤0,001) on the yield of GA is shown in Table. 3. Increasing the dynamic time has a negative quadratic effect (P≤0,01), and the negative interaction effect of P - dynamic time (P≤0,001) is more important. Researchers obtained similar results in this study; it is observed that after some time (103 min) the yield of GA does not increase at all and begins to fall. The reduction in yield refers to the fact that after achieving maximum recovery at the optimal conditions of 10 MPa, 60,2^{0}C, 103 min and 1,74 ml/min using RSM, GA recovery decreases due to the loss of mass transfer driving force (difference in GA concentration between mobile phase (SC-CO_2) and stationary phase (licorice petals) in the tube. Thus, the decrease in extraction seems to be expected and practically logical in terms of the transport phenomenon. The same effect mentioned is also predicted by RSM, in which the properties of the 2nd order polynomial equation are indicated on the negative terms T, quadratic T, P and dynamic time, as well as the influence of the interaction P - dynamic time.



(a)



(b)

Fig. 5. Dependence of the surface (a) and contour (b) for GA extraction as a function of the coded values of T (^{0}C) and dynamic time (min) at P = 10 MPa and a CO_2 flow rate of 1,3 ml/min.

3.2 Main and interacting effects of factors

Due to the presence of a multivariate effect acting on the output, the main effect, (Fig. 6), is obtained using the RSM model. This plot shows the average response at the level of each factor and is used in predicting the size of main effects. That CO_2 flow rate (Q) and dynamic time (min) have a positive effect and that T has a negative effect and that P first has a positive and then a negative effect on the output of GA is shown in Fig. 6. The interaction effect between operational variables (obtained from RSM) is shown in Fig. 7, where the deviation of parallel lines indicates interaction effects. As the table shows. 4 interactions T – P and p – dynamic time have a positive and negative effect value ($0{,}001 \leq P < 0{,}01$), respectively, on the extraction yield [20-31].

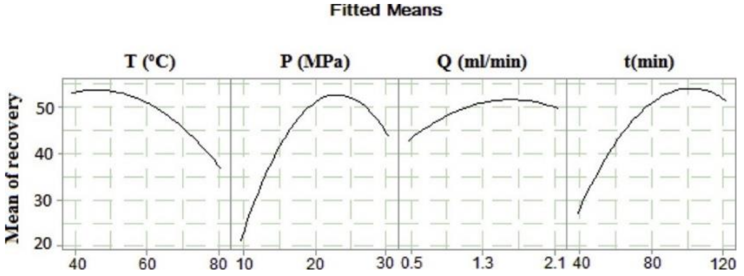


Fig. 6. Effects of interactions between operational parameters on GA recovery obtained using the RSM model.

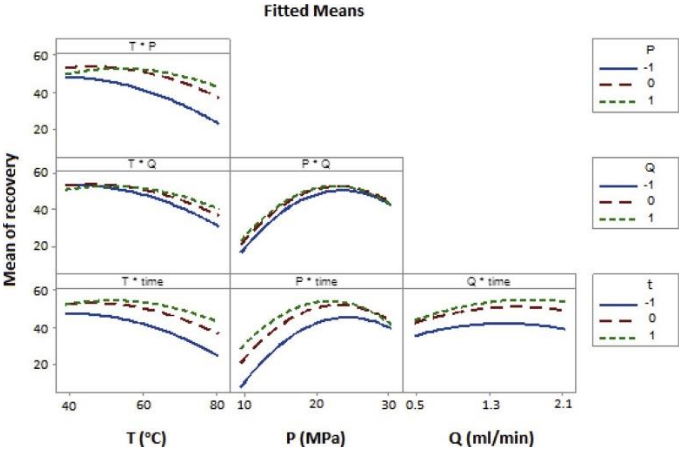


Fig. 7. Interaction effects between the operating parameters on glycyrrhizic acid recovery obtained by RSM model.

3.3 Optimizing operating conditions using RSM

The RSM (RESPONSE SURFACE METHODOLOGY) model predicts optimal conditions for SC – fluid extraction of GA. A maximum GA recovery of 56,18% (yield 2,20% (v/v)) is predicted through the RSM model under the optimal operating conditions: 21,0 MPa, 60°C, 1,70 ml/min and 100/min.

4 Conclusion

The extraction of GA from licorice roots is went by the SCFE strategy. The adjusted RSM impact of 4 autonomous factors (P, T, CO_2 stream rate and dynamic time) at five levels was surveyed and the yield could be a 2nd arrange show with R_2=95,66%. RSA affirms that the information are enough fit by a 2nd arrange polynomial show. The ideal working conditions ought to be 10,5 MPa, 60,5°C, 1,85 ml/min and a dynamic time of 100 min is anticipated utilizing RSM. Applying these working conditions, the most extreme GA surrender ought to be 56,4 %. The most extreme optimization for GA surrender is 55,4% at 10 MPa, 55,6 ^{0}C, 150 ml/min. These expectations of the two models are affirmed by triplet tests giving an normal abdicate of 54,8 ± 1,4% and 54,2 ± 1,3% for RSM and GA, individually, as watched, there is great understanding between the two optimization strategies.

Note: In arrange to calculate the legitimacy of the legitimacy, analysis of organized factors (ANOVA), loss of test affectability and leftover plot are embraced within the extra record.

References

1. S.M. Ghoreishi, E. Heydari, J. Supercrit. Fluids **74** (2013) 128-136.
2. S.M. Ghoreishi, E. Heydari, J. Supercrit. Fluids **72** (2012) 36-45.
3. K.Kh. Gafurov, A.F. Safarov, *Mathematical model of mechanical calculation of parts and assemblies of an experimental installation for CO_2 extraction* Materials of the rep. conference. “Modern problems of modeling mechanical and technological processes based on high technologies” (Bukhara-2013)
4. K.Kh.Gafurov, Sh.U.Mirzaeva, B.T.Muhamadiev, Butlerov Communications 11, vol. **48**, 35-39 (2016)
5. B.T.Muhamadiev, K.H.Gafurov, Sh.U.Mirzaeva, M.F.Sharipova, *Speed of extraction of lipids from melon seeds with supercritical CO_2 with co-solvent*, Chemical Journal of Kazakhstan, pp. 169-176 (Almaty, 2016)
6. Sh.U.Mirzaeva, B.T.Muhamadiev, K.Kh.Gafurov, K.E. Ruzieva, V.N. Akhmedov, Modeling of different extraction modes with a solvent system of ethanol + CO_2, Scientist of the 21st century, (publishing house Colloquium LLC, Yoshkar-Ola, 2017)
7. A. Bogdanovich et.al., The jour. Super. Fluids. **07**. 44-50 (2016)
8. Safarov A.F., Gafurov K.Kh. The use of liquefied carbon dioxide as a solvent for the production of extracts from plant materials (review). (Bukhara. 2014)
9. S.M. Ghoreishi et. al. Chem. Ing. Technol. **35 (1).** 133-141 (2012)
10. B. Kauftmann et. al. Phytohem. An. **18**. 70-76 (2007)
11. P. Kraulis, P.R. Venskutionis. Jour. Supercrit. Fluids. **73**. 178 (2013)
12. H. Matlab, Z. Sadat, A. Hezave. Jour. Supercrit. Fluids. **73**. 108 (2013)
13. L. Mokhtari, S.M. Ghoreishi, Jour. Supercrit. Fluids. **30**. 21 (2019)
14. Gafurov K.Kh., Mukhamadiev B.T., Mirzaeva Sh.U., *CO_2 extraction: problems and prospects,* “Development of science and technology” scientific and technical journal, (Bukhara 2014)
15. Kasyanov G.I., Korobitsyn V.S., Rokhman S.V. *Installations for supercritical CO2 extraction,* Sub- and supercritical fluid technologies in the food industry, Proceedings of the international scientific and technical Internet conference (Krasnodar 2012)
16. K.Kh. Gafurov, B.T. Muhamadiev, Sh.U. Mirzaeva. Butlerov communications 1, **49**. 108-114 (2017)
17. K. Gafurov, B. Muhammadiev, Sh. Mirzaeva, F. Kuldosheva. Food science and technology, Scientific and Production Journal Odessa, **14**. 1, 47-53 (2020)
18. X.F. Djuraev, K.Kh. Gafurov, B.T. Muhamadiev, Zh. Zhumaev, Sh.U. Mirzaeva. The American journal of applied science **2**, 273-286 (2020)

19. Sh.U. Mirzaeva. International Journal of Advanced Research in Science, Engineering and Technology **6,** 4, 8939-8946 (2019)
20. K. Gafurov, B. Muxamadiev, Sh.U. Mirzaeva, Production ingredients from plant raw materials by CO_2 extruction, (Lambert Academic Publishing, Monograph, 2018)
21. Sh.U. Mirzaeva, K.Kh. Gafurov, Zh. Zhumaev. Certificate of official registration of the program for electronic computers Optimization of the process of obtaining CO_2 extract from licorice root DGU 09833, 01.05.2021.
22. S.V. Butto, G.I. Kasyanov, V.S. Korobitsyn et.al., Using the extraction properties of liquid carbon dioxide to extract valuable components from plant materials. (Krasnodar: KubSTU, 1998)
23. Kasyanov G.I. Prospects for CO_2 technology in the processing of plant raw materials // In collection. abstract report intl. scientific conf. "Advanced technologies and equipment in the food industry." (Krasnodar: KubSTU, 1994)
24. Kasyanov G.I. // Izv. universities Food technology **2-3**. 72-75 (1998)
25. Kasyanov G.I. *Resource - and energy-saving technologies for storing and processing agricultural products using compressed and liquefied gases// In collection. mater, int. scientific-practical conf.* "Food industry of the South of Russia", Part 1.-Krasnodar: (KNIIHP, 2000)
26. Kasyanov G.I., Sagaidak G.A. // Izv. universities Food technology **2-3**. 85-86 (2001)
27. Stasyeva O.N., Latin N.N., Kasyanov G.I. CO_2 extracts from the Karavan company. – (Krasnodar: KNIIHP, 2003)
28. Shazzo R.I., Kasyanov G.I. // Storage and processing of agricultural raw material **3.** 10-13 (1999)
29. B.I. Leonchik, L.G. Alexandrov, G.I. Kasyanov, V.P. Kriulin // News of universities. Food technology **1.** 136-139 (1997)
30. X.F. Juraev, K.Kh. Gafurov, B.T. Muhammadiev, Sh.U. Mirzaeva, *Supercritical CO_2 extraction of glycyrrhizic acid from licorice root: optimization of extraction conditions using RSM (response surface methodology),* Science News of Kazakhstan, scientific and technical journal, Kazakhstan, **4,** 55-72 (2019)
31. Sh.U. Mirzaeva, Zh. Zhumaev Improving the process of licorice root extraction in a CO_2 environment (Durdona Publishing House, Monograph 2023)