EJMI

DOI: 10.14744/ejmi.2022.54474
EJMI 2022;6(1):70–77

Research Article

Determining the Length of Stay in the Intensive Care Unit of Patients With Sepsis Who Underwent Hemoadsorption Using the Artificial Neural Networks Model

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Abstract

Objectives: The artificial neural network (ANN) analysis was used to predict the exact staying period of patients with sepsis have undergone hemoadsorption hospitalized in the General Intensive Care Unit (ICU) of X University Hospital.

Methods: ANN model was successfully developed having 21 neurons in total (11 neurons at the first level, 9 neurons at the second level, and 1 neuron at the third level) using a computer program. The created network was trained using our real data and the fermi function of the system was determined by the program and then the program was able to predict possible staying time prior to real-time.

Main variables of interest: Staying periods (days), ages, number of comorbidities, hemoperfusion periods (days), blood pH, C-Reactive Protein, procalcitonin, and blood lactate levels were inputs.

Results: Predicted values were plotted to real data and the determination coefficient was found to be r2= 0.802. This relation was found to be good to predict the possible staying times of patients with sepsis treated using hemoadsorption in the ICU for a better organization and reducing the total cost.

Conclusion: The artificial neural network modeling and this prediction were found to be useful for predicting patients staying time at ICU.

Keywords: Artificial Neural Network, Intensive Care Unit, Hemoadsorption, Sepsis

Cite This Article: *Koc S, Uysal H. Determining the Length of Stay in the Intensive Care Unit of Patients With Sepsis Who Underwent Hemoadsorption Using the Artificial Neural Networks Model. EJMI 2022;6(1):70–77.*

Sepsis is defined by a dysregulated host response to infection as life-threatening organ dysfunction and is the leading cause of global loss of health, accounting for 19.7 percent of deaths in 2017.[1] As a method of blood purification, hemoperfusion (hemoadsorption column) is the passing of blood through a column or cartridge (covered with a thin, relatively porous, semimeable membrane) containing resin and activated charcoal. Adsorption occurs due to the hydrophobic properties of coal. It is more effective than hemodialysis in removing high protein binding and fat soluble drugs.[2] Thus, blood purification using HA330 cartridge-directed hemoadsorption is an emerging approach to alleviateing the cytokine storm and its harmful effects in the patients with sepsis. ANN modeling may be also useful to understand the patients with sepsis and its consequences. This approach may be interpreted by other disciplines for a better understanding of mortal diseases and its management in hospitals.[3]

In this study, we analyzed the correlation between the comorbidity, CRP, pH and PCT parameters of patients with

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Submitted Date: January 01, 2022 **Accepted Date:** February 04, 2022 **Available Online Date:** February 28, 2022

sepsis who underwent hemoadsorption column and the length of stay in general ICU using ANN modeling. This is the first time ever application for estimating possible staying periods of patients prior to realization.

Methods

Patients Selection Rules and the Setting

The 200 patients who met the diagnostic criteria for sepsis and were treated in the general intensive care unit of the X University Hospital (Istanbul, Turkey) were included in this study. Patients who did not meet the diagnostic criteria for sepsis according to ''The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3, in 2016)"[4] and/or did not undergo HA-330 hemoadsorption were excluded.

HA 330 Cartridge-Directed Hemoadsorption in the Patients with Sepsis

This therapeutic method is an electrically neutral microporous resin that is a efficient blood purification method in the clearance of "cytokine storm" occurred in the patients with sepsis and treated using HA-330 resin-directed hemoadsorption in general ICU.[5]

Development of an Artificial Neural Network (ANN) Model

ANN models are being increasingly used in medical and pharmaceutical researches to predict the nonlinear relationship between causal factors and response variables.[6] ANN model is described below for predicting staying time in general ICU of the patients with sepsis treated using HA-330 resin-directed hemoadsorption. ANN model is a computer algorithm inspired from biological systems and their working methodology. It is designed to learn from data in a manner emulating the learning patterns of the brain. Most ANN systems are quite complex, multi-dimensional, and nonlinear information processing systems.[7,8] ANNs are composed of hundreds of single processing artificial neurons. Artificial neurons are connected to each other with coefficients (weights), which constitute the neural structure, and are organized in sets of layers, mainly the input layer, output layer, and hidden layers in between. Neural networks obtain their knowledge by detecting patterns and finding relationships from the given data and they are trained through experience with appropriate learning examples.[9] The input layer neurons obtain data and the output neurons produce ANN's response. The parameters that affect the staying periods (days) of sepsis patients in ICU of X Hospital were evaluated by using an ANN analysis. ANN models were developed using selected input parameters such as ages, number of comorbidities, hemoperfusion periods (days), blood pH, CRP, PCT, and lactate levels where the staying periods (days) of sepsis patients in general ICU of X University Hospital was an output parameter. A computer program, Phytia, was used to develop ANN models (The Neural Network Designer version 1.0-Runtime Software LLC; Carson City, NV).[10] Computer program gave the best configurations and number of neurons at each level for predicting staying periods of sepsis patients. 11.9, and 1 neurons at each levels, from 1st to 3rd respectively: the average was found to be SSD=0.001356 after training. The best network model was developed using the optimizer and ANN models that achieved the lowest square deviations.

ANN calculations have two phases. Initial phases referred as "training phase" and the last one is the "reproduction phase". When training phases is completed, the network and each neuron got the exact value for fermi function and during the reproduction phases parameters are set and they do not change anymore. In back propagation networks, each neuron has one output and as many inputs as neurons in the previous level. Each network inputs is connected to every neuron in the first level. Each neuron output is connected to every neuron in the next level. The network's output is the output of the last level neurons. The network is processed from left to right in the given model.[11,12]

Results

The data of 200 registered patients with sepsis included in our study were uploaded to the computer program. The real data obtained from the unit and gave to the computer as initial parameters in this study. The computer program gave 11 neurons for the first level, 9 neurons for the second level, and one neuron for the third level, as the most suitable model for the prediction (SSD = 0.001356). ANN findings showed that the computer program made predictions successfully and the relationships between parameters were found to be complex. These complex relationships were defined successfully by ANN and estimations were conducted rapidly after system training. The interpretation of the effects of each descriptor parameter is difficult because the model is multivariate and nonlinear. However, some insight into the degree of nonlinear behavior of the descriptors has been assessed with a functional dependence to understand the relationships. The value of the input variables was varied through its range, whereas some others were roughly constant. The network output was plotted against two input descriptors to generate a functional dependence surface but that gives quite complex responses between input variables but there was not seen any clear and easily understandable relationship. However,

the real data and the predicted values were in the scope of predictability (Fig. 1 and Table 1). As an example, program predicts 16.65 staying days in ICU for the hypothetical patient who have input parameters (age=75, number of comorbidities=3, hemoperfusion periods (days)=5, blood pH=7.4, CRP=200, PCT=10, and lactate levels=3). It is similarly 60.02 days when only CRP values changed to 100 and it is given as 17.69 when CRP input is given as 300. According to these results it seems that CRP protects patient to stay longer in general ICU which is quite unexpected. When age increases (same data set as in first example, only age increased up to 90) program predicts patient to stay in general ICU for 17.56 days (Fig. 2).

Discussion

Numerous humoral indicators have been reported in the current literature that play a role in the prognosis and the length of stay in the hospital of patients with sepsis and / or septic

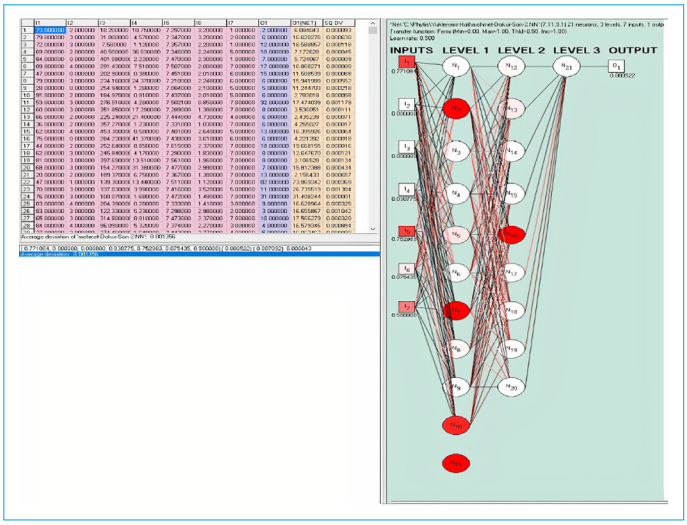

Figure 1. The schematic illustration of developed ANN model in the patients with sepsis who underwent HA-330 resin-directed hemoadsorption.

Note: The used parameters are given in Table 1 (n=200).

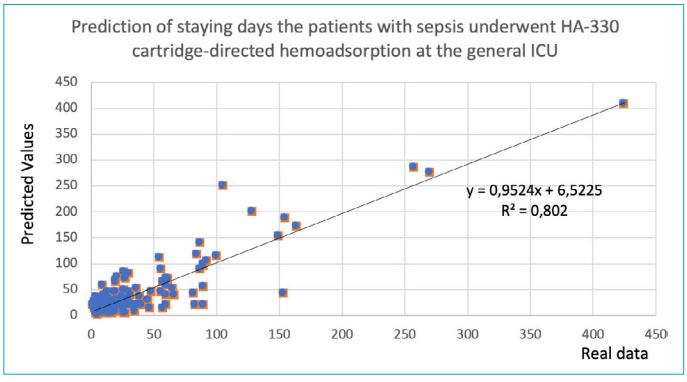

Figure 2. The relationship between real and predicted values.

shock. Among these, CRP, PCT, acidosis and blood lactate levels are the best known.[13,14,16] Consistent with this knowledges, in this study, we investigated the effect of parameters that are prognostic for sepsis on the length of stay in ICU.

In current treatment, methods that provide blood purification are becoming increasingly important. Among these hemoadsorption is an effective treatment method against the negative effects of sepsis-induced cytokine storm for patients treated in intensive care.[17] We used HA330 cartridge-based hemoadsorption method to reduce the effects of cytokine storm in patients with sepsis in this study.

Besides, accordingly the information supplied by Xu et al. corroborates the two small randomized controlled trial (RCT) results. Investigating the HA-330 resin-directed hemoadsorption adjuvant in septic patients with acute injury to the lungs. This theraphy compared to controls and in plasma and lung tissue, hemoadsorption treated patients had a significantly lower infammatory cytokine 'load'.[5,15] In a study in which Kulkarni et al. evaluated the prolonged hospitalization periods of patients hospitalized in the coronary intensive care unit after angiography, they showed that the longer the poor prognostic indicators increased, the longer the hospitalization periods.[18]

In our study, the most suitable ANN models were computed and developed for predicting the staying periods (days) of 200 patients with sepsis patients who underwent HA330 resin-directed hemoadsorption in General ICU of X University Hospital. The used computer program Phytia uses back propagation networks to achieve the best model. The parameters of network (weigths) are initially set random values. During the training phase the actual outputs compared with the desired (real outputs and the error value propagated back toward the input of the network. A special feature of the program called evolutionary optimiser. This option of the software automatically generates suitable networks and can find the best one for given data. The program achieves this considering the lowest square deviations.[10]

It seems that the blood parameters are deadly important to fight cytokine storm in the patients with sepsis underwent HA330 resin-directed hemoadsorption. All results showed that developed and trained ANN model is useful to predict of optimal staying period of critical patients' length of stay in ICU and relationships between parameters were found to be complex. Although these complex relationships were present and make prediction difficult when other ordinary methods used; our estimations were found to be rapid and feasible after easy system training and parameter input.

The developed and described ANN model in this publi-

Table 1. The used parameters for the prediction of the staying periods (days) of the patients with patients in ICU of X Hospital (n=200)

Age	Co-mobidities	CRP	PCT	pH	Lactat	Hemoperfusion duration (Days)	Days stayed in ICU
73	2	18,2	10,75	7,297	3,2	1	2
79	3	31,8	4,57	7,347	3,2	2	6
72	3	7,5	1,12	7,357	2,2	1	12
69	2	40,5	36,63	7,346	2,24	5	10
84	0	401,08	2,22	7,47	2,3	1	7
89	4	291,43	7,51	7,507	2	7	17
47	0	202,9	0,38	7,451	2,01	6	15
79	3	234,16	24,37	7,21	2,24	6	6
28	0	254,94	1,28	7,084	2,1	5	5
91	2	184,97	0,91	7,437	2,01	5	6
53	3	276,51	4,2	7,502	0,85	7	32
60	3	351,85	17,29	7,289	1,38	7	8
66	2	225,24	21,4	7,444	4,73	4	6
36	2	357,27	1,23	7,331	1,03	7	6
62	4	453,3	8,5	7,401	2,64	5	13
75	0	284,23	41,37	7,438	3,61	6	6
44	2	252,64	8,85	7,615	2,37	7	18
62	3	245,84	4,17	7,29	1,83	7	8
81	3	397,69	13,51	7,561	1,96	7	8
68	3	154,27	31,38	7,477	2,99	7	7
20	2	189,37	6,75	7,367	1,38	7	13
47	1	139,3	13,44	7,511	1,12	7	82
70	3	337,03	3,99	7,416	3,52	5	11
76	3	100,07	1,68	7,472	1,48	7	31
83	4	204,39	0,2	7,333	1,41	3	9
83	3	122,33	5,23	7,298	2,98	2	3
65	3	314,8	8,01	7,473	2,37	7	10
84	4	96,09	5,32	7,374	2,27	3	4
27	3	274,46	1,64	7,442	2,77	4	5
84	3	139	2,3	7,553	1,05	7	90
67	4	50,75	7,47	7,319	1,25	2	12
78	3	202,09	3,7	7,298	2,2	3	38
62	3	444,59	1,17	7,484	1,54	3	14
84	1	187,15	5,09	7,522	2,3	1	4
74	3	244,67	4,76	7,559	0,95	7	9
66	3	99,99	4,41	7,433	1,23	7	12
44	3	263,15	5,94	7,496	1,19	7	10
77	1	381,92	37,89	7,213	3,78	7	12
61	2	154,88	21,17	7,561	4,64	7	9
81	4	274,07	27,67	7,408	1,63	7	7
67	2	392,04	3,49	7,525	1,62	3	5
60	2	367,76	3,91	7,51	0,96	5	7
67	3	90,48	17,96	7,453	3,01	4	5
54	3	203,69	33,79	7,45	1,38	7	58
86	4	187,01	3,2	7,368	0,87	7	16
52	1	135,43	2,52	7,45	3,05	7	10
74	4	87,5	2,08	7,359	2,2	5	20
76	1	374.16	7,13	7,528	1,19	7	21
75	1	431,73	3,4	7,24	3,2	2	26

Table 1. CONT.

Age	Co-mobidities	CRP	PCT	pH	Lactat	Hemoperfusion duration (Days)	Days stayed in ICU
79	1	256.99	5,19	7,398	2,35	4	67
52	3	145,8	11,68	6,837	3,5	1	8
82	4	64,25	68,74	7,456	2,3	7	84
51	2	263.85	4,67	7,213	2,2	7	164
47	1	177,81	3,89	7,472	0,85	7	60
46	0	237,8	1,39	7,464	2,62	5	60
69	3	197,3	1,37	7,675	6,12	7	37
81	2	176,7	4,14	7,24	0,91	6	35
91	3	11,2	1,06	7,423	1,86	4	9
85	3	201,2	1,72	7,479	2,2	6	9
87	3	79,8	1,01	7,475	1,7	5	5
75	3	138.60	0,36	7,459	1,2	2	22
70	3	92,2	2,11	7,513	2,08	7	62
83	2	59.40	3,11	7,494	4,81	7	20
71	1	213,4	10,17	7,374	3,25	7	39
103	1	124,8	6,84	7,493	0,94	7	15
59	1	255,3	1,05	7,604	1,85	7	150
74	2	317,6	27,18	7,542	0,2	7	30
59	3	205,5	6,1	7,341	2,3	4	32
83	2	144,4	14,45	7,566	1,61	7	30
63	3	292,7	7,34	7,34	2,83	1	10
37	1	200,3	100,66	7,418	4,75	5	20
78	4	284,2	1,48	7,674	2,75	7	90
51	2	264,4	0,35	7,466	0,96	7	28
84	4	322,1	4,2	7,46	1,98	7	46
69	4	237,9	0,78	7,346	5,46	7	60
75	2	174,5	2,14	7,563	1,17	7	62
60	1	138	0,29	7,504	1,33	7	56
74	2	57,6	1,02	7,399	2,9	7	60
47	2	120,6	54,22	7,206	1,67	3	4
68	2	196	11,68	7,403	2,2	7	85
66	4	>340	43,83	7,379	2,29	7	12
70	2	287	24,85	7,588	3,99	7	47
59	2	>340	5,5	7,575	1,4	7	15
74	3	311	1,49	7,509	1,72	3	33
76	4	75,9	4,55	7,433	2,3	3	8
59	4	165,8	18,27	7,607	1,7	7	14
33	2	289,7	35,1	7,508	2,49	4	8
60	3	311,6	9,52	7,536	1,41	7	20
88	1	373,3	1,77	7,414	2,3	3	9
57	1	133.20	20,15	7,236	2,35	5	27
68	1	168,1	1,51	7,533	2,53	4	3
63	2	309,3	7,7	7,421	2,99	1	18
78	3	241,1	2,38	7,545	1,47	7	21
79	4	318,6	14,64	7.453	1,82	7	4
73	2	36	0,11	7,593	1,63	7	20
58	1	171,6	4,35	7,487	0,9	7	270
87	2	108,9	23,63	7,556	3,2	7	14
50	3	166,5	3,98	7,366	1,02	6	21

Table 1. CONT.

Age	Co-mobidities	CRP	PCT	pH	Lactat	Hemoperfusion duration (Days)	Days stayed in ICU
73	3	189	23,4	7,33	2,13	5	9
53	1	>340	5,15	7,612	3,09	5	90
48	0	130,3	1,14	7,545	1,57	7	17
58	4	>340	23,77	7,344	1,34	8	18
59	4	163,3	5,91	7,393	8,88	7	55
70	4	>340	36,08	7,502	0,98	7	10
80	2	266,7	31,69	7,267	3,15	8	30
76	1	115,5	100,49	7,331	1,4	3	5
71	3	227	2,75	7,531	0,95	9	17
81	3	110,5	0,21	7,477	0,87	7	20
87	4	226,9	45,97	7,343	2,2	7	11
77	3	265,4	35,88	7,531	2,32	5	21
79	1	189,9	5,13	7,352	3,07	7	9
62	4	183	14,03	7,336	2,2	3	17
74	2	103,1	9,03	7,44	1,46	7	20
45	3	122,6	16,21	7,329	2,1	7	26
43	2	138,8	49,58	7,312	2,2	7	14
80	4	>340	99	7,319	1,95	5	6
79	3	114	14	7,367	3,38	4	7
67	3	126	3	7,407	1,91	5	6
95	3	289,7	8,66	7,333	2,5	6	65
72	5	157	33,11	7,265	0,74	7	10
78	4	121,3	3,88	7,449	0,85	7	16
83	0	136,1	8,25	7,442	0,88	7	60
54	4	203,8	1,58	7,24	2,49	7	25
61	2	89,1	2,23	7,323	1,44	4	4
60	1	240,6	88,35	7,539	8,05	2	3
57	2	291,5	21,48	7,147	10,54	3	4
69	1	283,7	4,71	7,504	1,13	7	30
47	2	84.30	1,53	7,276	0,68	4	5
58	3	304,3	28,92	7,302	1,27	2	5
51	1	283,5	100.89	7,408	0,98	7	16
83	1	241,5	9,68	7,59	1,06	7	14
69	4	198.10	2,87	7,608	1,14	7	40
52	1	247.30	1,18	7,506	2,15	7	9
78	3	91,7	2,26	7,34	3,62	7	21
77	2	84,3	2	7,495	2,24	7	27
95	3	113,2	8,16	7,333	2,5	6	30
72	4	157	33,11	7,265	0,74	7	9
83	0	136,1	8,25	7,442	0,88	7	58
25	0	108	10,81	7,545	0,73	7	28
54	4	203.50	1,58	7,24	2,49	7	17
75	3	138,6	0,36	7,459	1,2	2	24
64	4	183,5	0,96	7,499	1,39	6	8
83	2	271,1	1,16	7,361	0,97	7	12
74	3	192	0,87	7,547	2,2	7	28
71	1	108	27,98	7,618	2,32	7	28
77	2	57,9	114,49	7,466	6,35	6	92
66	4	194,3	10,37	7,22	3,07	6	5

Table 1. CONT.

Age	Co-mobidities	CRP	PCT	pH	Lactat	Hemoperfusion duration (Days)	Days stayed in ICU
54	1	127,5	0,96	7,528	0,78	7	105
87	3	310,5	2,33	7,371	1,76	6	10
56	4	274,8	0,98	7,252	1,28	7	24
80	2	83,3	9,31	7,547	1,19	5	129
74	4	142	45,56	7,262	1,12	7	18
90	3	218,8	3,09	7,577	2,79	7	19
57	3	>340	27,64	7,354	1,63	7	11
65	2	>340	2,31	7,522	0,88	6	20
92	3	184,3	70,3	7,502	1,13	7	155
76	2	304,5	2,58	7.454	3,14	6	87
74	3	68,8	3,46	7,405	2,66	6	257
73	3	329	1,33	7,531	2,47	7	87
67	2	140.60	64,19	7,57	1,31	7	9
71	4	102,2	26,95	7,416	1,11	4	6
80	1	194,1	9,4	7,397	2,12	7	11
76	4	178,4	1,89	7,334	1,65	5	13
75	3	177,4	2,33	7,556	1,34	7	153
88	4	228,3	16,28	7,568	1,53	4	6
70	1	>340	1,73	7,557	2,03	3	13
75	2	143,7	24,54	7,476	3,02	7	56
79	3	293,8	9,97	7,574	2,98	7	60
65	2	234,8	45,14	7,391	2,42	7	13
68	4	161.80	11,5	7,434	2,02	4	32
54	4	145,3	3,04	7,422	2,52	7	16
79	3	162,1	4,51	7,522	1,7	3	8
65	4	289,2	12,81	7,384	2,22	5	8
84	2	252,9	1,13	7,455	2,29	2	5
55	0	>340	4,59	7,412	1,58	10	16
75	3	106,5	4	7,504	1,35	11	24
73	2	129	1,18	7,449	1,15	7	25
33	1	>340	8,06	7,378	1,39	7	26
58	3	348,8	35,26	7,392	0,69	4	101
76	2	138,6	2,72	7,433	2,2	7	90
73	2	15,7	1,2	7,645	6	4	24
59	1	193,2	0,17	7,458	0,52	4	425
68	3	125,8	47,8	7,402	1,11	3	37
64	2	118,3	1,91	7,417	1,23	2	4
82	2	175,1	0,83	7,393	1	4	21
74	5	198,5	56,03	7,309	1,29	5	6
86	3	262,6	9,88	7,266	1,01	4	25
68	3	130,1	1,02	7,564	1,05	7	48
79	3	181,4	4,48	7,578	2,08	6	20
73	2	45	2,22	7,156	3,53	7	21
75	4	182,8	3,14	7,09	2,11	6	9
75	3	140,3	1,35	7,428	0,93	7	30
55	0	295,2	9,49	7,458	1,83	4	12
61	3	210,3	13,72	7,425	1,4	7	30
79	2	81,8	7,47	7,441	3,28	5	5
80	2	208,3	10,18	7,205	2,3	7	15

Table 1. CONT.

Age	Co-mobidities	CRP	PCT	pH	Lactat	Hemoperfusion duration (Days)	Days stayed in ICU
62	2	239,3	3,19	7,546	1,59	7	14
62	2	73,2	0,28	7,235	0,54	7	21
84	0	>340	3,63	7,468	0,98	6	5
60	3	191,9	2,37	7,417	2,3	6	

CRP: C-Reaktif Protein; PCT: Procalcitonin; ICU: Intensive Care Unit.

cation does not require any experimental parameters; it could potentially provide useful and precise prediction or information about the patients with sepsis that may be useful any further possible fatal diseases. This can be easily adapted to other data and studies.

Disclosures

Ethics Committee Approval: The study protocol was permitted by X University Faculty of Medicine Ethics Committee (Permission No: 2019/27-14). The study was completed according to the mandates of the Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – S.K., H.U.; Design – S.K., H.U.; Supervision – S.K., H.U.; Materials – S.K., H.U.; Data collection &/or processing – S.K.; Analysis and/or interpretation – H.U.; Literature search – S.K., H.U.; Writing – S.K., H.U.; Critical review – S.K., H.U.

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