REVIEWER 1
Comments and Suggestions, and Answers

We are very grateful for the valuable opinion and comments. All the suggested valuable changes have done in the corrected version of our paper.

1) ,,keywords should not be limited only to listing the research material and the methods used - suggests correcting, they do not facilitate the search for the topic of work''

Answer for Reviewer

As suggested by the Reviewer the keywords was change.

New version:

gum arabic; tragacanth; proper storage conditions; UV-irradiation; higher temperature; relative humidity; TGA; c-DTA; colorimetric analysis; UV spectrophotometry; optical microscope observations

2) ,,line 32-35 - too generally described influence of air / ambient humidity on API durability''

Answer for Reviewer

As suggested by the Reviewer in the Introduction was extended described influence of air / ambient humidity on API durability.

,,The active pharmaceutical ingredient or excipients may be decomposed by the hydrolysis process by the action of steam or water [10]. The derivatives of carboxylic acids (esters, lactones, lactams, amides) show the greatest sensitivity to this type of reaction [11]. Moisture can also influence on crystalline system of APIs [12,13]. This applies especially to unstable or metastable amorphous forms which, under the influence of increased humidity, tend to change the internal order consisting in reaching the form with the lowest internal energy [12]. This may alter the release profile of the drug or influence on bioavailability of the drug substance [11, 13]. Increased moisture sorption by the finished drug formulation may cause an increase in microbial contamination [14]. Also substances sensitive to increased humidity or light can be decomposed by oxidation [15]. Particularly sensitive to oxidation reactions are thiols, thioethers, ethers, aldehydes, but also natural gums [11]. Oxidation processes are often accompanied by a change in color or odor, which makes them easier to observe [11].''

[10] Tomar, M.; Singh, A.K.; Sinha, A.R. Effect of moisture content of excipient (microcrystalline cellulose) on direct compressible solid dosage forms. *Int. J. Pharm. Sci. Res.* **2017**, 8(1), 282-288.
[11] Sznitowska, M (Ed.). Farmacja Stosowana; PZWL: Warsaw, Poland, 2017; pp. 795, 798, 896, 925.
[12] Prudic, A.; Ji, Y.; Luebbert, C.; Sadowski, G. Influence of humidity on the phase behavior of API/polymer formulations. *Eur. J. Pharm. Biopharm.* **2015**, 94, 352-362.
[13] Rumondor, A.C.F.; Stanford, L.A.; Taylor, L.S. Effects of polymer type and storage relative humidity on the kinetics of felodipine crystalilization from amorphous solid dispersions. *Pharm. Res.* **2009**, 26(12), 2599-2606.

[14] Tomar, M.; Singh, A.K.; Sinha, A.R. Power and tablet profile of microcrystalline cellulose (MCC) of different with degree of polymerization. *Int. J. Rec. Sci. Res.* **2016**, 7(6), 12044-12047.
[15] Hovorka, S.W.; Schoneich C. Oxidative degradation of pharmaceuticals: theory, mechanisms and inhibition. *J. Pharm. Sci.* **2001**, 90(3), 253-269.

3) ,,fig 3c i 4c harmonize graphically with figs 3a/4a and 3b/4b''

Answer for Reviewer

As suggested by the Reviewer the figures 3c, and 4c was deleted.

4) ,,Table 1 and 2 line "Storage conditions" L * [± 0.05] ??? what is reading is this a standard deviation? Such presentation of the results raises doubts about the reliable measurement or their conversion. Even if for each of the parameters L * a * b there is the same value of the standard deviation ... which I strongly doubt, it should be taken into account for each of the parameters.''

Answer for Reviewer

The results are presented as standard deviation (±SD). For each parameter, the maximum standard deviation obtained for all results was originally given. However, as indicated by the Reviewer, a change was made and the standard deviation was given for each parameter separately.

5) ,,Fig 5 describing A should start with 0 - negative values indicate analytical errors, although the fact of the appearance of a value below zero but close may also be the issue of the sensitivity of the spectrophotometer ...''

Answer for Reviewer

As indicated by the Reviewer, the figure 5 has been corrected.

6) ,,it is necessary to correct the section "3.4. Impact of relative humidity, temperature, and time on water vapor sorption", in principle, two concepts of humidity levels are doubled - vapor sorption in water. In addition, there is no description of how the relative air humidity is controlled. There are also explanations why the measurements were made in a strange and, as for me, randomly selected temperature of 25 degrees Celcius for 45% RH and 75% at 40 degrees C for 65% RH - no consistency.''

Answer for Reviewer

As indicated by the Reviewer, the section 3.4. has been corrected.

,, *3.4. Impact of relative humidity, temperature, and time on vapor sorption*

In this studies the correct drug storage conditions defined by the standards [43], i.e. room temperature 25°C (±2°C) and relative humidity (RH) below 60% (±5%) were used. The temperature of 25°C, and RH of 45% were chosen, as these are the values most often found in drug warehouses in Poland [44]. In addition, drug storage parameters defined as abnormal were used. Two types of inappropriate conditions have been selected. Proper temperature (25°C) and

elevated RH (75%) and improper temperature (40°C) and elevated RH (65%).

Natural polymers in the form of a thin layer of powder were placed in Petri dishes and placed in an incubator with constant parameters: 25°C (±2°C)/RH 45% (±5%), 25°C (±2°C)/RH 75% (±5%), and 40°C (±2°C)/RH 65% (±5%). Relative humidity (RH) values were controlled using a hygrometer produced by Fisher Scientific (Suwanee, Ga, USA).''

[43] Guide to good storage practices for pharmaceuticals Annex 9, *WHO Technical Report Series, No. 908*, World Health Organization, **2003**

[44] Kucharczyk, M.; Slusarski, B. Mapowanie rozkładu temperatury w przestrzeniach magazynowych – praktyczne podejście. *Farm. Pol.* **2009**, 65(10), 707-712.

In addition, other researchers [1-4] testing polymers used in their works, inter alia, applied temperature conditions (25°C, 40°C), and RH (45%, 65%, 75%) in different compilations.

[1] Rumondor, A.C.F.; Stanford, L.A.; Taylor, L.S. Effects of polymer type and storage relative humidity on the kinetics of felodipine crystalilization from amorphous solid dispersions. *Pharm. Res.* **2009**, 26(12), 2599-2606.
[2] Rumondor, A.C.F.; Taylor, L.S. Effect of polymer hygroscopicity on the phase behavior of amorphous solid dispersions in the presence of moisture. *Molecular Pharmaceutics* **2009**, 7(2), 477-490.
[3] Collier, J.W.; Shah, R.B.; Gupta, A.; Sayeed, V.; Habib, M.J.; Khan, M.A. Influence of formulation and processing factors on stability of levothyroxine sodium pentahydrate. *Pharm. Sci. Tech.* **2010**, 11(2), 818-825.
[4] Marsac, P.J.; Konno, H.; Rumondor C.F.R.; Taylor, L.S. Recrystallization of nifedypine and felodipine from amorphous molecular level solid dispersions containing poly(vinylpyrrolidone) and sorbed water. *Pharm. Res.* **2008**, 25(3), 647-656..

7) ,,3.7. Analysis of UV-Vis spectrophotometry - why does UV-Vis appear in the title if the wavelength (nm) 200-380 is UV?''

Answer for Reviewer

As indicated by the Reviewer, the title of chapter 3.7. has been corrected.

8) ,,applications should be written in continuous text, without bullet points 1-6,''

Answer for Reviewer

As indicated by the Reviewer, the Conclusions were reorganized.

,,The performed examination of influence of different physical factors like UV-radiation, higher temperature, and relative humidity during storage of gum arabic and tragacanth pointed out that GA is more resistant to higher temperatures compared to GT. Thermogravimetric dynamic analysis (TGA) and c-DTA showed a two-step decomposition both polimers. The first stage is related with the release of absorbed water by GA and GT. The second step is related to the complete decomposition of the tested samples. Moreover, thermogravimetric isothermal analysis (TGA) showed the greatest mass lost for gum tragacanth, and gum arabic were recorded at temperature 50°C and 60°C respectively.

The storage temperatures (40°C-80°C) used in experiment indicated no or a barely visible color change in system CIE L*a*b* . This indicates the relative resistance of the tested polymers to the applied temperature conditions. It is additionally confirmed by the recorded UV spectra and the optical microscopy images.

The evaluation of the influence of UV-radiation on GA and GT, analytical methods used at work, shows the relative stability of the tested polymers. Slightly larger changes were recorded for gum arabic compared to tragacanth. Which may indicate potential changes in GA under the influence of UV-radiation.

The largest assessed changes occurred in GA and GT under the influence of storage conditions in high relative humidity. Polymers stored in high relative humidity (75% RH) showed the highest weight loss in TGA isothermal measurements. It proves high water sorption by the samples under these conditions. Colorimetric analysis showed a significant color change in the system CIE L*a*b* of polymers exposed to high relative humidity (75%RH/25°C) and high relative humidity and temperature (65%RH/40°C) in relation to the initial samples. This indicates changes occurring in the tested polymers as a result of their exposure to the tested physical factors. The most visible changes in the optical microscopy images were visible for the samples stored under the conditions of 75% RH/25°C/3 days. Especially this observations concerned for gum arabic.

UV absorbance spectra for GA showed a hypochromic effect for all storage conditions. In turn, only GT stored under conditions 75% RH/25°C/3 days showed a hyperchromic effect.''

9) ,,line 340 - UV-VIs ???''

Answer for Reviewer

As indicated by the Reviewer, the UV-Vis in line 340 has been corrected.