Electronic supplementary information

Materials and methods

Flow-ability parameters of AVH

Angle of repose

Angle of repose was calculated to determine the flow property of a material and estimation of frictional forces among particles. Fixed funnel method was used to calculate angle of repose (Equation (1)) (Lachmann et al., 1987). The height of the funnel was fixed and AVH was permitted to pass through this fixed funnel on a flat surface until the apex of formed heap just touched the lower tip of funnel.

$$\text{Tan}\,\theta = \frac{h}{r} \tag{1}$$

where, θ, is angle of repose, h is the height of the formed heap and r is the radius of that heap.

Bulk and tapped density

Measurement of bulk density (D_b) of AVH was accomplished by filling accurately weighed (W_h) AVH (1.0 g) in graduated cylinder (10 mL) and noted the filled volume (V_b). For tapped density (D_t), filled cylinder was allowed to fell from a height of 3 cm on hard board for 100 times and noted the packed volume (V_t) of AVH. Bulk and tapped density of AVH were calculated using Equation (2) and (3), respectively (Lachmann, 1987).

$$D_b = \frac{W_\text{h}}{V_b} \tag{2}$$

$$D_t = \frac{W_\text{h}}{V_t} \tag{3}$$

Hausner ratio and Carr's index

Hausner ratio (H) and Carr's index (C) of AVH were estimated to assess its flow property and packing arrangements which are essential for a material to be used as an inactive pharmaceutical ingredient. The value of Hausner ratio and Carr's index more than 1.25 and 25 are considered as a poor flow material, respectively. Hausner ratio and Carr's index was determined using Equation (4) and (5), respectively (Lachmann, 1987).

$$Hausnerratio(H) = \frac{D_t}{D_b} \tag{4}$$

$$Carr's\ index(C) = 100\left(1 - \frac{D_b}{D_t}\right) \tag{5}$$

where, D_t and D_b are tapped and bulk density of AVH, respectively.

Moisture content of AVH

To analyze moisture content of AVH, weighed sample (1.0 g) was shifted to vacuum oven for 1 h at 105 °C and determined the weight of sample again. Moisture content is the difference

Evaluation of pre- and post-compression parameters

Lubricated granules are evaluated for pre-compression parameters before compression. Granules are tested for angle of repose, bulk density, tapped density, Hausner ratio and Carr's index. After compression, tablets were evaluated through post compression parameters, i.e., content uniformity, hardness, thickness, friability and weight variation. The results of all pre- and post-compression parameters are within the standard range. Angle of repose, Carr's index, Hausner ratio, weight variation, hardness, thickness and friability were found in the range of 26.72°, 14.76, 1.14, 4.1– 4.8%, 7.1– 7.8 kg/cm^2, 3.92– 3.98 mm and 0.84-0.93 %, respectively.

Results and discussion

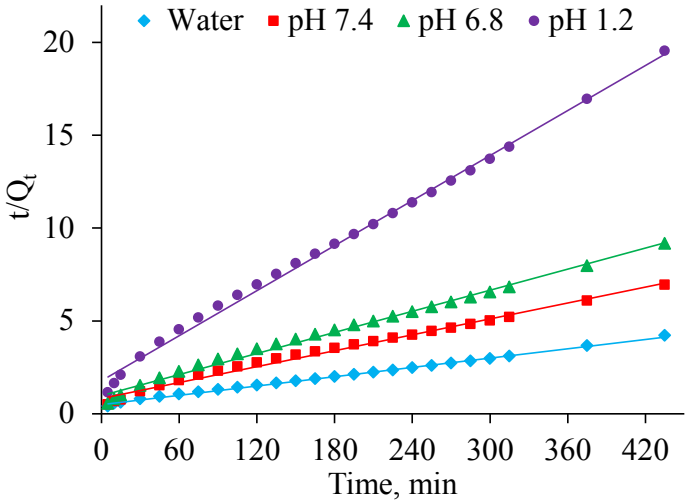

Fig. 1S Swelling kinetics of AVH at pH 1.2, 6.8 and 7.4, and in deionized water.

Table S1. Different ingredients used in the formation of AVH matrix tablets.

Constituents (mg/tablet)	**ACF1**	**ACF2**	**ACF3**
AVH	150	200	250
ACF	100	100	100
Microcrystalline cellulose	105	55	05
Tragacanth gum	40	40	40
Magnesium stearate	05	05	05

Table S2. Scheme for acute oral toxicity of AVH in rats.

Group I	Group II	Group III	Group IV
Control group of rats fed with standard diet	Treated group of rats fed with AVH (50 mg/kg body weight) mixed with diet	Treated group of rats fed with AVH (300 mg/kg body weight) mixed with diet	Treated group of rats fed with AVH (2000 mg/kg body weight) mixed with diet

Table S3. Physical parameters of AVH.

Physical properties	Results
Moisture content (%)	8.3 ± 0.60
Average Particle size (μm)	≈ 253
Angle of repose	43.7 ± 0.67
Bulk density (g cm^{-3})	0.25 ± 0.17
Tapped density (g cm^{-3})	0.33 ± 0.12
Carr's index (%)	24.3 ± 1.25
Hausner ratio	1.32 ± 0.07
Swelling capacity (g g^{-1}) after 24 h	102.06 ± 5.21

Table S4. Mathematic values of Power-law for formulations ACF1-ACF3.

Formulation code	***n***	***Kp***	R^2
ACF1	0.889	14.613	0.9979
ACF2	0.907	11.728	0.9921
ACF3	1.064	7.292	0.9964

Table S5. Body weight, and food and water intake of treated and untreated group of rats.

Parameters	**Group I**	**Group II**	**Group III**	**Group IV**
Body weight (g)				
Pretreatment	191.67±2.9	179.33±4.1	163.04±4.1	177.32±3.8
Day 1	186.11±3.0	175.01±3.8	159.23±1.7	173.28±2.7
Day 2	187.15±4.4	177.73±4.4	157.67±2.2	171.11±1.8
Day 3	188.47±5.6	179.33±3.9	159.01±3.5	170.59±3.1
Day 5	190.33±3.9	181.21±2.9	163.4±4.8	172.51±1.9
Day 7	194.35±3.9	183.41±3.2	165.7±2.3	173.22±2.4

Day 9	193.22±2.9	184.64±2.1	164.2±4.1	175.71±3.6
Day 11	194.33±2.5	185.52±2.7	167.7±2.3	176.29± 2.1
Day 14	193.37±2.8	185.71±3.5	166.2±3.4	178.55±2.65
Water intake (mL)				
Pretreatment	9.11±1.13	8.16±1.59	7.58±2.10	7.85±2.20
Day 1	8.79±1.33	5.61±2.03	4.09±1.73	6.41±1.70
Day 2	8.63±1.38	7.91±2.07	7.33±2.04	7.91±0.90
Day 3	9.03±1.0	8.01±2.08	7.51±2.12	7.81±1.2
Day 4	10.41±2.11	10.217±2.31	8.59±1.83	7.91±1.5
Day 14	10.52±2.17	10.35±2.76	8.67±1.73	7.52±0.88
Food intake (g)				
Pretreatment	6.01±1.43	8.13±2.04	6.63±1.04	7.92±0.68
Day 1	5.91±1.23	4.85±1.39	2.96±1.23	3.02±1.1
Day 2	5.03±1.38	5.11±1.37	3.31±.92	4.74± 0.97
Day 3	6.19±1.74	5.95±0.88	5.47±1.59	5.21±1.0
Day 4	7.11±1.78	7.89±1.29	6.18±1.49	7.5±1.3
Day 14	6.22±2.05	8.54±1.53	7.28±1.02	8.02±0.87

Table S6. Absolute organ weight of rats.

Organs	Group I	Group II	Group III	Group IV
Heart	0.343±0.01	0.361±0.02	0.397±0.01	0.385± 0.03
Kidney	0.665±0.02	0.689±0.01	0.677±.02	0.693±0.02
Stomach	2.07±0.2	2.161±0.01	2.277±.03	2.379±0.05
Pancreas	0.257±.01	0.221±0.01	0.229±0.01	0.221±0.03
Lungs	0.603±.01	.581±0.01	0.575±.001	0.588±0.02
Intestine	7.225±0.6	6.659±0.2	6.709±0.2	6.925±0.41
Liver	5.645±0.4	5.409±0.3	5.611±0.2	5.724±0.24

References

L. Lachmann, H. A. Liberman, J. L. Kanig, Theory and practice of industrial pharmacy, third ed., Lea and Febiger, Philadelphia, 1987.