Formulation and evaluation of antioxidant tablet using gallic acid as active phytoconstituent

Authors name: Jain A., Fulmali S.* Govalkar P., Amkar A.

Institution: Shri D.D. Vispute College of Pharmacy & Research Center, New Panvel

Corresponding Author: Dr. Sushama Fulmali

Assistant Professor of Pharmaceutical Science

Shri D.D. Vispute College of Pharmacy & Research Center,

New Panvel, Navi Mumbai 400049

E mail: sushamafulmali@gmail.com

Tel no: Phone:+91 8108590290

Tital: Formulation and evaluation of antioxidant tablet using gallic acid as active phytoconstituent

Abstract:

From ancient time, man has been depending on plants as medicine. Oxidation processes is among the most common problem associated with various disease, affecting a large proportion of the world's population. These diseases can be treated by using various herbal drugs. The purpose of the present work was to formulate antioxidant gallic acid tablets so that a particular dose of antioxidant to be reached in the target sight. In this work, gallic acid was used, which was obtained from the market. The different tablets were prepared by using different types of disintegrating agents and various excipients. The granules of the gallic acid were prepared by a wet granulation technique using microcrystalline cellulose. The blends were evaluated for flow properties and for compressibility, which were found to be good. The tablets were prepared using a single rotatory punching machine, in which the punch size was 11 mm×8 mm, and formulated wet granulated tablets. The compressed tablets were evaluated for weight variation, thickness, hardness, friability, in-vitro drug release using USP dissolution apparatus. The optimized Formulation table of formulations F5 formulation was found to be acceptable because it release drug up to 5.3403 % of drug release for gallic acid tablet and this batch passed all the evaluation parameters.

1. Introduction:

Plants are always a rich source of drug. In fact, many of the currently available drugs were derived either directly or indirectly from the plants. The plant kingdom represents a good source of organic compounds, many of which have been used for medicinal and other purposes.[1] Herbal medicine remains the major source of health care for the world's population. Gallic acid (3, 4, 5-trihydroxybenzoic acid) is a naturally occurring polyphenolic compound found in processed beverages such as red wines and green teas. It is widely distributed across the plant kingdom such as leaves (beriberry), roots and bark (pomegranates and nuts).[2] It is also found in some hard wood plant species such as *Teminalia chebula, Castanea sativa, Mangifera indica* L and many other.[3] Gallic acid is a yellowish white crystal having a molecular mass of 170.12 g/mol, melting point 250 °C and water solubility 1.1% at 20 °C.[4] It can be synthesized from phenylalanine via caffeic acid or trihydroxycinnamic acid.[5]. It is well known for its natural and strong anti-oxidative, anti-mutagenic, anti-carcinogenic, anti-allergic, anti-inflammatory anti-viral, anti-bacterial, anti-arteriosclerosis activities.[6, 7] Pro-oxidant property of gallic acid has been recognized as the apoptosis inducer in cancer cell lines.[8]

The problems of conventional herbal tablet were the improper dosing and unpredictable absorption of the drug led to us to the concept of controlled drug delivery system. The goal behind these delivery systems is to reduce the frequency of dosing and to increase effectiveness of the gallic acid by localization of the drug at the site of action which in turn reduces the dose requirement and thus provides uniform drug delivery. The rational of active phytoconstituent drug delivery is to ensure safety and to improve effectiveness of drug and thus improve patient's compliance also.

2. Material and Methods:

Gallic acid was obtained from gift sample from exporter lab chemical , andheri , Mumbai . starch cellulose , MCC , croscarmellose , aerosil were collected from college laboratory. All other chemicals were used of Analytical grade.

2.1 Method of Granule preparation:

Accurately weigh Gallic acid, Starch cellulose, Microcrystalline cellulose and Croscarmellose. And then passed all the ingredients through 40 mesh size sieve. Then prepared a dough mass and passed through 8 mesh size sieve. Then it passed through 20 mesh size sieve supported on 40 mesh size sieve. Granules retained on 40 mesh size are collected and fines equal to 10% of weight granules is added along with previously weighed aerosol. And then dried in oven for 180 ^{0}C for 30 min.

2.2 Formulation of Different Batches

Table1: Shows different batches prepared by taking different concentration of ingredients

Ingredient (mg)	Fi 1	Fi 2	Fi 3	Fi 4	Fi 5
Gallic acid	100	100	100	100	100
Microcrystalline Cellulose	10	14	18	22	26
croscarmellose	12	14	16	18	20
Aerosil	4	4	4	4	4
Starch cellulose paste (10 %)	150	150	150	150	150

2.3 Evaluation of Flow Properties of Granules

2.3.1 Angle of repose

5g Granules were poured through the walls of a funnel, which was fixed at a position by clump with stand such that its lower tip was at a height of exactly 2cm. above from plan surface. The granules were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. Θ= tan-1 (h/r) Θ= angle of repose, h = height of the heap, r = radius of the heap

2.3.2 Bulk density and Tapped density

Granules were poured gently through a glass funnel into a graduated cylinder. The cylinder was then tapped from a height of 2.0 cm. until the time when there was no more decrease in the volume. Bulk density and Tapped density was calculated.

Bulk density = Weight of sample in g/final volume in cm3 of the sample contained In cylinder Tapped density=Weight of sample in g/final volume in cm3 after tapped in cylinder 2.3.3 Carr's compressibility index (C.C.I.): Used for compare the bulk Density and tapped density. Carr's compressibility index=Tapped density--bulk density/tapped densityX100 2.3.4 Hausner's ratio: Hausner's ratio= Tapped density/Bulk density

Table 2: Different Pre-compression parameters of both the layer of bilayer tablet

Formulation Code	Angle of Repose (Ɵ)	Bulk Density (g/cm3)	Tapped Density (g/cm3)	Carr's Index (%)	Hausner's Ratio
F1	22.10	0.3289	0.3614	8.93	1.125
F2	19.01	0.3901	0.4014	2.81	1.025
F3	15.75	0.4432	0.4723	6.16	1.048
F4	24.61	0.4481	0.4791	6.49	1.069
F5	26.15	0.4693	0.5028	6.66	1.071

2.4 Evaluation of prepared Tablets

2.4.1 Weight Variation: The USP provides the weight variation test by weighed 20 tablets individually, calculated the average weight and compared the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the % limit and if no tablet differs by more than 2 times the % limit.

2.4.2 Hardness and Friability Hardness of tablets measured by Monsanto hardness tester. A pre-weight tablets sample is placed in friabilator which is then operated for 100 revolutions for 4 minutes. After test tablets that lose less than 1.0 % of their weight are generally considered acceptable.

Table 3: Comparison of physical parameters of tablet obtained by wet granulation techniques

Formulation Code	Friability (%)	Hardness (kg/cm2)
F1	1.1613	5.2
F2	0.8911	4.6
F3	1.0210	3.8
F4	0.9524	4.0
F5	0.99	3.5

2.5 In -Vitro Dissolution Studies for gallic acid

1. The release rate of Gallic acid tablet was determined by using USP dissolution testing apparatus 2 (Paddle type).
2. The dissolution test was performed using 900 ml of 0.1 N HCL, at 37 + 0.5 C and 50 rpm.
3. Aliquot 10 ml volume was withdrawn from dissolution apparatus at time interval 0,5,10,15,20,25,30,35,40,45,50 and samples are replaced with fresh dissolution medium.
4. After filtration and suitable dilution the amount of drug release is determined from the calibration curve.

Table 4: In vitro Drug Release Studies of F5 of gallic acid

Sr. No	Time(min)	% CDR
1	0	0%
2	5	5.2224%
3	10	5.2090%
4	15	5.2744%
5	20	5.2912%
6	25	5.312%
7	30	5.3403%

3. Result and Discussion

3.1 Evaluation of flow properties of granules of gallic acid

Prepared granules were evaluated for their flow a property is Angle of repose (θ) ranged from 22.10 to 26.15 with granules prepared by wet granulation technique. It shows good flow property of prepared granules. Carr's index (CI) obtained were in the range of 6.66 to8.93 and Hausner's ratio (HR) observe in the ranged from 1.071 to 1.12. for granules in the different formulations. These value show good flow property of prepared granules.

3.2 Weight variation

The weight variation was observed for different formulations with low standard deviation value, including uniformity of weight. The variation was carried when it was range of ± 5 % complying with pharmacopoeia specification (Indian Pharmacopoeia 1996). All tablets passed weight variation test.

3.3 Hardness: The hardness of all formulations was observed and it revealed in the range from 3.5 to 5.2 kg/cm2.

3.4 Friability-The percentage friability of all formulations were observed and it was in the range from 0.99 % to 1.16 %.

3.5 In Vitro drug release of gallic acid: By increase the concentration of super disintegrating agent the % drug release (gallic acid) is increased. F5 has highest 5.3403 of gallic acid release so It was considered as best optimized formulation

4. Conclusion

The overall result of the present work shows that this formulation of gallic acid shows the calculated release of its from prepared tablet. The various concentration of MCC was used to formulate a formulation which sustained the release of gallic acid for7 hours. The reason behind choosing the MCC because it works as binder cum diluent for the delivery system, MCC provide several advantages i.e. sustained release, good stability in varying pH values and moisture levels.

This could be concluded after performing all the evaluations that if we formulate a sustain release gallic acid tablet by varying its mode of release as per the biopharmaceutical property of the drug. We can increase the bioavailability of the formulation. At the End of the of the dissertation work a active phytoconstituent tablet of gallic acid is the best promising mode of delivery for getting its good antioxidant property.

5. Acknowledgement

Author is thankful to Dr Ashish Jain Head Department of Pharmacy to provide research facility

6. Reference

1. Choubey, S., Varughese, L. R., Kumar, V., & Beniwal, V. (2015). *Medicinal importance of gallic acid and its ester derivatives: a patent review. Pharmaceutical Patent Analyst, 4(4),*
2. Ahmad I, Aqil F, Owais M. Modern phytomedicine: Turning medicinal plants into drug. Weinheim: Wiley-VCH Verlag; 2006: 27-30.
3. Mizukami Y, Sawai Y, Yamaguchi Y. Simultaneous analysis of catechins, gallic acid, strictinin, and purine alkaloids in green tea by using catechol as an internal standard. Journal of Agricultural and Food Chemistry 2007; 55(13):4957–4964.
4. Friedman M, Jurgen HS. Effect of pH on the stability of plant phenolic compounds. Journal of Agricultural and Food Chemistry 2000; 48(6): 2101–2110.
5. Badhani B, Sharma N, Kakkar R. Gallic acid: a versatile antioxidant with promising therapeutic and industrial applications. RSC Advances 2015: 5(35): 27540–27557.
6. Choubey S, Varughese LR, KumarV, Beniwal V. Medicinal importance of gallic acid and its ester derivatives: a patent review. Pharmaceutical Patent Analyst 2015; 4(4): 305–315.
7. SoongY, Barlow P. Quantification of gallic acid and ellagic acid from longan (*Dimocarpus longan* L.) seed and mango (*Mangifera indica* L.) kernel and their effects on antioxidant activity. Food Chemistry 2006; 97(3): 524–530.
8. Bharti Badhani, Neha Sharma and Rita Kakkar, Gallic acid: a versatile antioxidant with promising therapeutic and industrial applications, RSC Adv. 2015,**5**, 27540-27557.
9. .
10.