Formulation of Herbal nanocapsules for the treatment of gastric problems

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Introduction

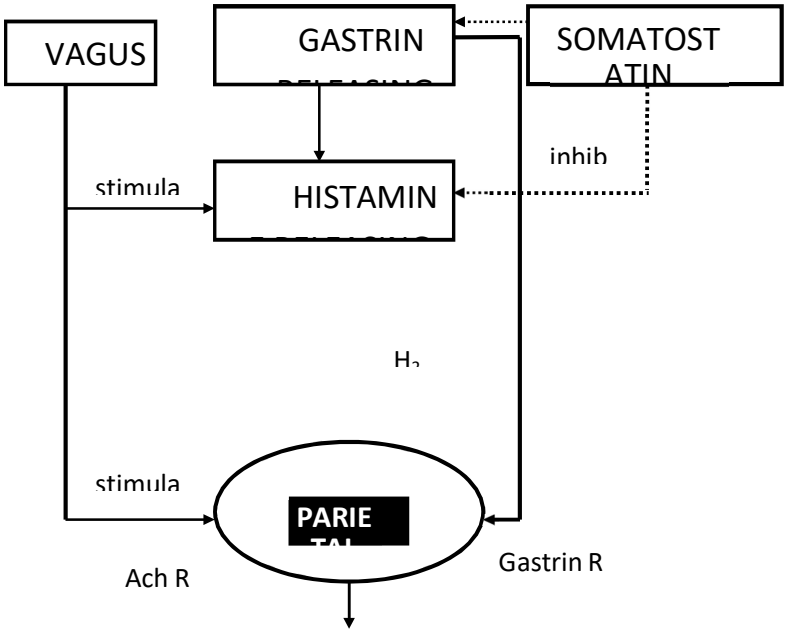
Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe. The herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. Although herbs had been priced for their medicinal, flavoring and aromatic qualities for centuries, the synthetic products of the modern age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security. Over three-quarters of the world population relies mainly on plants and plant extract for health care. More than 30% of the entire plant species, at one time or other were used for medicinal purposes. Human being appears to be afflicted with diseases more than any other animal species. [1]Thus he very early sought to alleviate his sufferings from injury and disease by taking advantage of plants around him. Today a vast store of knowledge concerning therapeutic properties of different plants has amassed. All phyla of plants contain species that yield official and unofficial products of medicinal importance. By far the greatest number of these are derived from plants.[2]

PEPTIC ULCER

The acid-peptic diseases are those disorders in which gastric acid and pepsin are necessary, but usually not sufficient, pathogenic factors.20 While inherently caustic, acid and pepsin in the stomach normally do not produce damage or symptoms because of intrinsic defense mechanisms. Barriers to the reflux of gastric contents into the esophagus comprise the primary esophageal defense. Peptic ulcers are craters or open sores in the lining of the upper gastrointestinal tract (GIT). [3]They include duodenal ulcers (those that are located in the top of the small intestine or duodenum) and gastric ulcers (those found in the stomach). Peptic ulcers are

common and usually occur singly. But it is possible to have two or more, or even both duodenal and gastric ulcers at the same time[4] Although the pathogenesis of peptic ulcer disease is not fully understood, three major factors are recognized: infection with gram-negative H. pylori, increased hydrochloric acid secretion, and inadequate mucosal defense against gastric acid. Treatment approaches include (1) eradicating H. pylori infection, (2) reducing secretion of gastric acid or neutralizing the acid after it is released, and (3) providing agents that protect the gastric mucosa from damage.[5]

Digestive system: Cross-section of the alimentary tube has four layers the mucosa, submucosa, external muscle layer, and serosa. Each layer has a specific structure, and its functions contribute to the functioning of the organs of which it is a part.



Acute ulcer

Usually associated with sepsis, injection (cytomegalo-virus) [CMV], Candida, tuberculosis [TB], syphilis), surgery/trauma, central nervous system (CNS) injury or disease (Cushing's disease), extensive burns (Curling's ulcer), use of drugs (aspirin, steroid), or after radiation therapy.

- ✓ If superficial, involving mucosa only (erosion), can heal completely

- ✓ If deep, fibrosis replaces muscle and perforation may occur

Microscopic

- ✓ Marked epithelial atypia

Chronic ulcer

- ✓ Cardinal symptom is nocturnal epigastric pain
- ✓ Associated with achlorhydria
- ✓ 95% along the lesser curvature
- ✓ 95% accuracy with endoscopic and 70% accuracy with radiographic diagnosis
- ✓ Questionable risk of malignancy Macroscopic
- ✓ 5% multiple
- ✓ Sharp delineation.

Causes of peptic ulcers

Peptic ulcers occur in 5-20% of long term NSAID use.

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are a group of medications typically used to treat pain. There are many drugs in this group. A few of these include: aspirin, oxaprozin. NSAIDs are also included in some combination medications,[5,6] such as Alka-Seltzer, Acetaminophen and is therefore the preferred non-prescription treatment for pain in patients at risk for peptic ulcer disease.[7] Because NSAIDs are so common, and because many are available over the counter without a prescription, they are a very common cause of peptic ulcers. NSAIDs cause ulcers by interrupting the ability of the stomach and the duodenum to protect themselves from naturally occurring stomach acid. NSAIDs also can interfere with blood clotting. This has obvious Importance when ulcers bleed.[8] People, who take NSAIDs for a long time, at high doses or both, have a higher risk of developing

ulcers. These people should discuss preventing ulcers with their physician.[9] A PPI can prevent or significantly reduce the risk of an ulcer being caused by NSAIDs.

PLANT COLLECTION

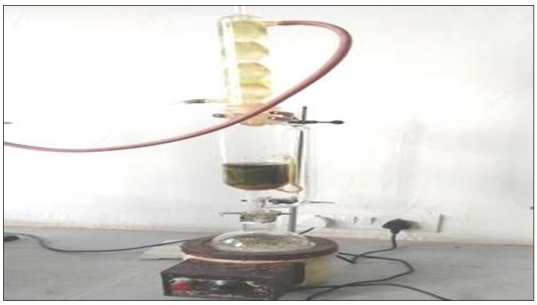
Aloevera and Citrus Lemon were collected from Botanical Garden Chandrapur. It was identified and authenticated by Nirmal Institute of Agriculture Technology Gondia 441614.

Preparation of extract:

Aloevera and Citrus Lemon were shade dried and then ground till they became coarse powder in a motar-pestle. The powdered material thus obtained was subjected to extraction using Petroleum Ether and Ethanol. The extracts obtained were distilled to remove excess of the solvent and then evaporated at 40oC to get a semi-solid mass.[10]

PROCEDURE

About 100 gm of powdered material of Aloevera, and lemon was extracted with water as a solvent by hot extraction method using Soxhlet apparatus. The extraction was continued until the solvent in the thimble became clear then few drops of solvent were collected in the test tube during the completion of the cycle and chemical test of the solvent was performed. After each extraction, the extract was evaporated to dryness some part of the extract was preserved for preliminary Phytochemical screening for the detection of various plant constituents and rest extract was used for formulation of gel batches.[11]



EVALUATION OF NANOCAPSULE

Drug entrapment efficiency of Nanocapsule

Entrapment efficiency of Nanocapsule was determined by centrifugation method. Aliquots (1 ml) of liposomal dispersion were subjected to centrifugation on a laboratory centrifuge (Remi R4C) at 3500 rpm for a period of 90 min. [12]The clear supernatants were removed carefully to separate non entrapped and absorbance recorded at 245nm. The sediment in the centrifugation tube was diluted to 100 ml with phosphate buffer pH 7.4 and the absorbance of this solution was recorded at 245 nm. % entrapment of drug was calculated by the following formula

$$\% \text{ Drug Entraptment} = \frac{\text{Drug Loading}}{\text{Theoratical Drug loading}}$$

Table No 1: Results of entrapment efficiency of Nanocapsule of formulations

Dissolution Batch Code			
Sr.No	**F1**	**F2**	**F3**
1	46.23	45.62	47.47
2	48.38	47.70	48.15
3	50.73	47.80	49.63
Mean	49.33	47.71	49.08
Mean ± S.D.	48.33±1.000	47.70±0.566	49.09±1.545

VESICAL SIZE

Table no 9: Vesicle size

Sr.no	Formulation	Size (μm)
1	F1	130
2	F2	142
3	F3	150

Table No 10: Results of particle size of Nanocapsule

Sr.No	**F1**	**F2**	**F3**
1	6.43	7.22	6.08
2	7.15	6.74	7.20
3	6.62	7.43	6.70
Mean	6.72	7.22	6.5

Mean ± S.D. 6.76±0.097 7.24±0.050 6.7±0.062

Now, let H0 be the hypothesis that there is no significant difference between the batches.

In Vitro Drug release study

The release studies were carried out in 250 ml beaker containing 100 ml Phosphate buffer. Phosphate buffer pH 7.4 (100 ml) was placed in a 250 ml beaker. The beaker was assembled on a magnetic stirrer and the medium was equilibrated at 37±50C. Dialysis membrane was taken and one end of the membrane was sealed. After separation of non entrapped liposomal dispersion was filled in the dialysis membrane and other end was closed. The dialysis membrane containing the sample was suspended in the medium. 5ml of aliquots were withdrawn at specific intervals, filtered after withdrawal and the apparatus was immediately replenished with same quantity of fresh buffer medium.

Table 2: Cumulative percentage drug release from various formulation of Nanocapsule

Time (HRS)	Batch code		
0	**F1**	**F2**	**F3**
1	17.38	19. 17	22.80
2	24.07	23.63	25.18
3	27.14	26.10	28.32
4	30.32	30.35	31.72
5	31.85	32.62	32.35
6	34.41	34.44	36.54
7	36.14	36.53	43.09
8	45.52	42.51	52.12
9	53.21	53.10	60.26
10	62.20	62.61	69.10
11	72.65	72.58	87.39
12	81.48	83.38	92.88

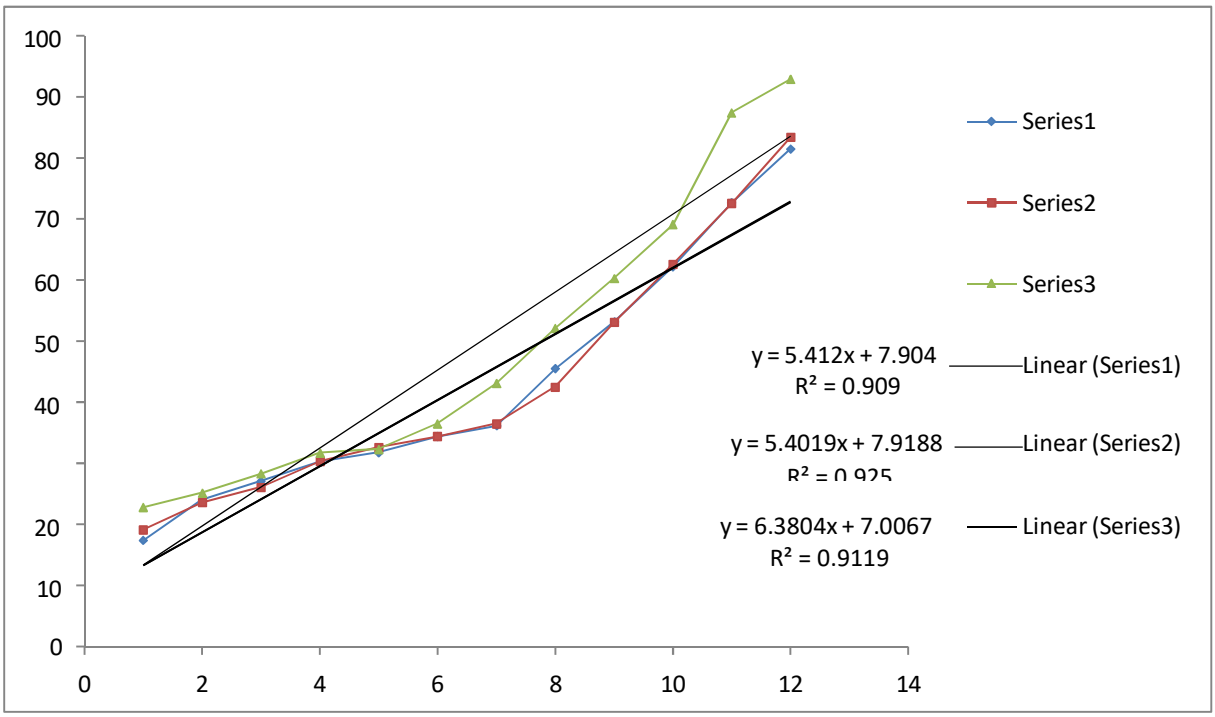


Figure 2 : in vitro drug release of various formulations

Zero order First order Peppas model

Sr.No	Batch Code			
1	F1	0.8350	0.9156	0.9420
2	F2	0.8623	0.8632	0.9217
3	F3	0.7965	0.8722	0.9422

Fig. 3. Order of reaction

RESULTS AND DISCUSSION

The aim of this study is to prepare the herbal extract loaded liposome formulation in that extract of Aloevera & Lemon plant is needed is to increase the availability of the encapsulated drug. To achieve this goal, Nanocapsule Thin lipid film- hydration method was used to prepare Nanocapsule.

PHYSICO- CHEMICAL CHARACTERISTICS

The Nanocapsule formulations were evaluated for their physico-chemical properties and found to be colorless and odorless. The liposomal hydrogels were also found to The liposomal formulations were be odorless, translucent and with neutral pH. The properties of formulations immediately and on 15 day did not show any differences in their properties indicating the physical stability of the formulations. The physic-chemical properties of herbal extract liposomal hydrogel complex suggest that it has a good potential for topical drug delivery. The other important criteria for selection of material in the complex development is, the selected components are pharmaceutically acceptable, non-irritating and non- sensitive to the skin and all the excipients fall under the GRAS category.

ENTRAPMENT EFFICIENCY (EE)

The amount of drug entrapped into the liposome and in Nanocapsule formulations was determined. The entrapment efficiency was in the range of 63.28 to 68.46 %. A good amount of drug was entrapped in the liposome formulations prepared.

DISCUSSION

In nearly every post commercial endeavors are highlighted implicitly and explicitly. For the week we observed “top” immune booster content on the concept of “immune boosting” was unequivocally portrayed as beneficial. Benefits included bettering mood and digestion, protection against a variety of infections and disorders, and improved skin and appearance. The most common actions to achieve an immune boost were food and diet related, while other actions included supplements, essential oils, exercises, sweating, and cold showers. A few posts included cautions about their immune-boosting advice. In general charged liposome’s were more stable against aggregation and fusion than uncharged liposome’s. However physically stable neutral liposome’s have been described. The inclusion of negatively charged lipid such as stearylamine tends to increase the entrapped volume. Show s the percent drug entrapment in various liposome

formulations. The release kinetics was found to be first order initially followed by mixed order. More drugs were released from charged liposomes than the neutral liposome's. A prolonged duration of response was observed during in vivo studies of liposome formulation. Positively charged liposome showed greater duration of action (DR 468 min) and AUC (23.5) compared to negatively charged liposome's (DR 11 hour) and AUC (12 hour) The results obtained are in accordance with the results obtained by Schaeffer. The reason may be the surface of the epithelial cell membrane is slightly negatively charged therefore, positively charged liposomes interact intensively with the surface. Weismann studied the atropine base entrapped in MLVs with a positive surface charge showed a prolonged effect up to 12 h whereas in solution form, the pupil dilation lasted for 7 h. MLVs with neutral and negative charges maintained the effect for 9 h. These studies demonstrated the importance of the liposomal charge in vesicle retention.

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