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NOVEL DRY INJECTION FOR RECONSTITUTION OF ASPIRIN USING SOLID SOLUBILISERS

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ABSTRACT

The concept of mixed solvency is an emerging field which can serve as a milestone for solubility enhancement and therefore deserves an urgent attention of the scientific community to assess its efficiency and applicability. Mixed solvency concept suggested that each substance present on the earth whether solid, liquid or gas has solubilizing power. In mixed solvency concept each substance (gas, liquid or solid) is termed as solubilizer. Solubility enhancement by a single solubilizer in high concentration may raise the toxicity concern. Mixed solvency concept gives solution to this problem. Several solubilizers in small concentration in a blend may give desired solubility for a given drug and hence may be safe (non-toxic). In future, the industries shall use the solubilising properties of different additives for such purpose. The described research is one typical example where safe concentrations of additives have been used to prepare a dry injection for reconstitution of aspirin (a poorly water soluble drug)

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INTRODUCTION:

As we know that all materials which exist in liquid state are known as solvents like water, chloroform, methanol, propylene glycol, dimethyl formamide, dimethyl sulfoxide, ethanol, benzene etc. No solvent is universal solvent. In other words, we can say that although these all liquids are known as solvent but they are not good solvents for all solutes. For example we know that water is good solvent for about one third drugs and bad solvent for about two third drugs. Thus we can say that all liquids are good solvent for some solutes and bad solvents for other solutes. Similarly, in mixed solvency concept [1] each and every substance (gas, liquid or solid) is good solubilizer for some solutes and bad solubilizer for other solutes.

MATERIALS AND METHODS:

Aspirin was procured as a gift sample from Shree Pharmaceuticals Indore. Lignocaine hydrochloride and niacinamide were procured from Modern Laboratories, Indore.

Experimental

Solubility studies

Approximate solubility studies were carried out to determine the solubilities of seven drugs in an aqueous blend containing safe solid additives of injection in safe concentration (reported in literature). The solubilising efficiencies of these additives were evaluated. The aqueous blend (B) contained 5% w/v sodium benzoate (a safe buffering agent), 5% w/v PVP K30 (a plasma expander), 2.5% w/v niacinamide (a safe stabilizer), 7.5% w/v PEG 4000 (a safe solubilizer) and 5% w/v lignocaine hydrochloride (a safe local anesthetic). Approximate solubilities of drug were determined by shaking the excess of drug with 10 ml of the blend for about 20 minutes in a bottle and then filteration was done. Approximately saturated solution of aspirin was analysed by titration with 0.1N NaoH using phenolphthalein indicator. For remaining drugs, spectrophotometric estimation were done. Approximate solubilities of all seven drugs are reported in Table 1.

Table 1 also gives solubilities of drug in distilled water at room temperature. Approximate solubility of aspirin in distilled water at room temperature was obtained by shaking excess of aspirin with about 60 ml of distilled water in a bottle for about 20 minutes. It was then filtered and filtrate was analyzed titrimetrically. Result is presented in Table 1. The solubilities of remaining six drugs were taken from research papers.

Out of seven drugs studies, aspirin was selected for further study. A model dry injection of aspirin was developed. Although aspirin has about 8.811% w/v solubility in the blend (B), an injection was developed having 5% w/v strength of aspirin. Thus 2ml of such solution contains 100 mg of aspirin.

Table 1: Solubilities and solubility enhancement studies

S.No	Name of drug	Solubility in distilled water at room temperature (% w/v)	Solubility in blend (B) at room temperature (%w/v)	Solubility enhancement ratio
1	Aspirin	0.331	8.811	26.6 fold
2	Norfloxacin	0.088	0.652	7.4 fold
3	Naproxen	0.009	5.745	638.3 fold
4	Tinidazole	0.538	1.206	2.2 fold
5	Piroxicam	0.040	0.994	24.8 fold
6	Frusemide	0.064	2.013	31.4 fold
7	Indomethacin	0.036	3.009	83.6 fold

Formulation development of dry injection

Approximate solubility of aspirin in distilled water is 0.33 % w/v at room temperature. Approximate solubility of aspirin in an aqueous solution (a mixed solvency blend) containing 5% w/v sodium benzoate, 5% w/v lignocaine hydrochloride, 5% w/v PVP K30, 7.5% w/v PEG 4000 and 2.5% w/v niacinamide is 8% w/v. Thus a 5% w/v solution of aspirin can be made easily in the above mentioned mixed solvency blend. Hence, 2ml of such solution shall contain 100 mg of aspirin. It is evident from the literature that 5% w/v sodium benzoate is safely employed buffering agent in injections. PVP K30 is a plasma expander; therefore, 5% w/v PVP K30 is safe in injections. In this case lignocaine hydrochloride is an additive (local anesthetic to reduce the pain of injection). PEG 4000, an additive (solubilizer) is safe in 7.5% w/v concentration in injections. Niacinamide (2.5% w/v) is a safely used stabilizer in injections. Thus, all five solid additives are present in safe concentrations in mixed solvency blend. Because of the solubilising effect of all five solids, the solubility of aspirin is enhanced tremendously and an aqueous injection can be developed to contain 100 mg aspirin in 2 ml of the blend. A dry injection of aspirin can nicely be developed to have very good chemical stability in the form of dry injection for reconstitution.

Table 2 gives a formula for model dry injection of aspirin. Aspirin, 100 mg (sieved through fine sieve), lignocaine hydrochloride, 100 mg (sieved through fine sieve), niacinamide, 75 mg (sieved through fine sieve), PEG4000, 150 mg (fine powder), sodium benzoate, 100 mg (sieved through fine sieve) and PVP K30, 100 mg (sieved through fine sieve) are kept in a 5ml vial. When 2 ml distilled water is added in the vial and vial is shaken vigourously, a clear solution is obtained. This experiment explains that a dry injection of poorly water soluble drug, aspirin, can be developed using solubilising power of all five solid solubilizers. Chemical stability studies and toxicological studies shall have to be performed to develop a drug injection for reconstitution of aspirin. All materials used in this formula should be free from pyrogens and microbes. Containers should be sterile and aseptic room shall be employed during its manufacture.

Table 2: Composition of model formulation

S.No.	Ingredients	Quantity
1	Aspirin (sieved through fine sieve)	100 mg
2	Lignocaine hydrochloride (sieved through fine sieve)	100 mg
3	PVP K30 (sieved through fine sieve)	100 mg
4	Niacinamide (sieved through fine sieve)	75 mg
5	PEG4000 (powder)	150 mg
6	Sodium benzoate (sieved through fine sieve)	100 mg

CONCLUSION:

Mixed solvency concept can further be utilized for development of dry injections as well as dry syrups of various poorly water soluble drugs. In above research work it is important to note that drug selected is a model drug and solublizers are model solubilizers. Formulations of various insoluble drugs can be developed using mixed solvency technique. Similarly, several combinations of safely used additives may be used to make innumerable safe blends giving enhanced solubilities of poorly soluble drugs.

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