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Research Article

EFFECT OF RED AND WHITE WINE ON DRUG RELEASE PATTERN FROM SUSTAINED RELEASE DOSAGE FORMS

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ABSTRACT

The main objective of SR formulations is to better control the magnitude and duration of drug action. Some modified-release oral dosage forms contain drugs and excipients exhibiting higher solubility in ethanolic solutions compared to water. Such products might be expected to have the potential to induce dose dumping in the presence of ethanol. Previous study by the authors evaluated the effect of alcoholic beverages like Strong beer, Mild beer, rum and 40% alcohol on the release profiles of sustained-release dosage forms containing Metformin and Diclofenac. The effect of wine remained unchecked till date. Hence, the objective of present study was to evaluate effect of red and white wine on the drug release pattern of sustained released dosage forms. The results of present study conclude that, in case of IR formulation, drug release was faster in red wine than white wine as compared to water. Similar results were obtained in case of SR formulations of Metformin and Diclofenac. As alcohol content of red wine is more than that of white wine, the results of present study indicate that the release of drug depended on concentration of alcohol.

KEY WORDS: Red wine, White wine, Metformin, Diclofenac, SR formulations.

INTRODUCTION

Sustained release (SR) formulations also referred to as extended release or controlled release typically contain the entire daily dose of a drug and are designed to steadily and continuously deliver this drug over an extended period of time. The main objective of SR formulations is to better control the magnitude and duration of drug action (Hoffman, 1998). Extended release dosage forms are the drug delivery systems of choice for the control of chronic diseases. The control over the release rate of drug is due to excipients such as hypromellose (hydroxypropyl methylcellulose), ethyl cellulose, etc which have varying but quantifiable solubility in alcohol. Hence, administration of such drug products along with consumption of alcohol may lead to dose dumping. Unintended, rapid drug release in a short period of time of the entire amount or a significant fraction of the drug contained in a modified release dosage form is referred to as 'dose dumping'. Depending on the therapeutic indication and the therapeutic index of a drug, dose-dumping can pose a significant risk to patients, either due to safety issues or diminished efficacy or both (Meyer and Hussain, 2005). One of the pharmacokinetic studies in healthy subjects, which demonstrated that co-ingestion of hydromorphone with 240 ml of 40% alcohol resulted in an average peak hydromorphone concentration approximately six times greater than when taken with water. This study also showed that 8 ounces of 4% alcohol (equivalent to 2/3 of a typical serving of beer) could in some subjects

result in almost twice the peak plasma hydromorphone concentration than when the drug was ingested with water. Some modified-release oral dosage forms contain drugs and excipients that exhibit higher solubility in ethanolic solutions compared to water. Such products may exhibit more rapid drug dissolution in the presence of ethanol. Therefore, in theory, concomitant consumption of alcoholic beverages along with these products might be expected to have the potential to induce dose dumping. This potential mechanism leading to dose-dumping from an oral modified-release dosage form has not attracted much attention in the pharmaceutical science literature (FDA, 2005).

Approximately 70 percent of the adult population consumes alcohol at least occasionally, and 10 percent drink daily (Midanik and Room; 1992). Alcohol content of wine range between 10-22 %. Alcoholic beverage consumption patterns vary considerably among different countries and even among different ethnic groups within one country (Linda ET AL., 198). Wine is most commonly use alcoholic beverages. The largest wine drinkers are the wine producing countries of Europe (WHO, 2005).Previous study by the authors evaluated the effect of alcoholic beverages like Strong beer, Mild beer, rum and 40% alcohol on the release profiles of sustained-release dosage forms containing metformin and diclofenac. The results demonstrated that the drug release of the sustained-release formulations was faster in 40% alcohol and in rum than it was in water (Joshi et al., 2010). However, the effect of wine remained unchecked till date. Hence, the objective of present study was to evaluate effect of red and white wine on the drug release pattern of sustained released dosage forms.

MATERIALS AND METHODS

Materials: Ethanol of analysis (40% v/v) was standard reagent grade (Baker, Germany), Wine (10-22% alcohol, South Seas Distilleries & Breweries Pvt. Mumbai, Maharashtra, India)

Drug Formulations:

1. Metformin Formulations-Metformin IR (Glycomet®-500, Batch No: 13003812) (USV Limited, Himachal Pradesh,), Metformin SR (Glycomet®-500 S.R. Batch No: 28002510) (USV Limited, Himachal Pradesh).

2. Diclofenac Formulations-Diclofenac SR (Voveran®- S.R 100 Batch No: 98033 A) (Novartis India Limited, Himachal Pradesh),

Diclofenac IR (Voveran®- 50, Batch No: 107015AD) (Novartis India Limited, Himachal Pradesh)

Dissolution study:

A) Metformin IR, SR(IP, 2007)**:**

Apparatus: USP Type I Dissolution Apparatus

Medium: De-mineralized water

Speed: 100 rpm

Six tablets from the same batch of each product were tested. The volume of de-mineralized water was 900 ml maintained at 37±0.5^{0}C. A suitable volume of medium was withdrawn, filtered and diluted with de- mineralized water and the amount of metformin released from the dosage form was determined using UV/ Visible Spectrophotometer (Shimadzu Model No.1700 E, EUROPE) at a wavelength of 233 nm. For the alcoholic dissolution study, the designated volume of alcoholic beverages was included in medium for 1 hour (volume made up to 900 ml using de-mineralized water) to simulate in vivo conditions. After 1 hour the medium was replaced with the fresh de-mineralized water at 37±0.5^{0}C. The same procedure was followed for determination of drug release in all solutions. The designated volumes of various alcoholic beverages are as follows:

Red wine: 60 ml

White wine: 60 ml

The data obtained were analyzed using PCP-DISSO software developed and supplied by Bharati Vidyapeeth College of Pharmacy, Pune-411038, Maharashtra, INDIA.

B) Diclofenac IR, SR :

Apparatus: USP Type I Dissolution Apparatus

Medium: De-mineralized water

Speed: 100 rpm (for Diclofenac SR)

50 rpm (for Diclofenac IR)

Six tablets from within the same batch of each product were tested. The volume of De-mineralized water was 900 ml maintained at 37±0.5^{0}C. The amount of Diclofenac released from the dosage form was determined using UV – Visible Spectrophotometer (Shimadzu Model No.1700 E, EUROPE) at a wavelength of 277 nm. For the alcoholic dissolution study, the designated volume of alcoholic beverages was included in medium for 1 hour (volume made up to 900 ml using de-mineralized water) to simulate in vivo conditions. After 1 hour the medium was replaced with the fresh de-mineralized water 37±0.5^{0}C. The same procedure was followed for determination of drug release. The designated volumes of various alcoholic beverages are as below:

Red wine: 60 ml

White wine: 60 ml

The data obtained were analyzed using PCP-DISSO software developed and supplied by Bharati Vidyapeeth College of Pharmacy, Pune.

RESULTS AND DISCUSSION

In present study, it was found that in case of IR formulation, drug release was faster in red wine and white wine as compared to water. Metformn IR formulation showed faster drug release in red wine (100%) than in white wine (88%) as compared to water (82%) at 15 min interval (figure 1). Diclofenac IR followed the same pattern with faster drug release in red wine (84%) than in white wine (62%) as compared to water (55%) at 15 min interval (figure 3). Similar results were obtained in case of SR formulations of Metformin and Diclofenac. Metformn SR formulation showed faster drug release in red wine (100%) than in white wine (88%) as compared to water (82%) at 8 hour interval (figure 2), while Diclofenac SR showed faster drug release in red wine (100%) than in white wine (92%) as compared to water (93%) at 8 hour interval (figure 4). Metformn SR formulation showed 100% drug release in red and white wine drug release compared to 97% drug release in water at 12 hour interval. The alcohol content of red wine is 13% and that of white wine is 8% as per the label. Thus, the results of present study indicate that the release of drug depended on concentration of alcohol. The consequences of the changes in the dissolution profiles observed in case of SR formulations would depend on the drug. In case of Metformin, dose dumping could result in anaphylactic reactions and lactic acidosis amongst other effects. In addition, Metformin is excreted by renal route in its unchanged form. Dose dumping could also result in renal impairment with Metformin. For Diclofenac, dose dumping could cause allergic reactions, fluid retention and impairment of renal function (Goodman and Gilman, 2001).

Low F2 values confirmed the significant changes in release pattern. The similarity factor *F*2 as defined by FDA is a logarithmic reciprocal square root transformation of one plus the mean squared (the ave rage sum of squares) differences of drug percent dissolved between the test and reference products (Gohel and Panchal; 2002). Table 1 gives the F2 values for the dissolution study n red and white wine against that in the plain water. This clearly indicates the effect of alcoholic beverages on in vitro drug release.

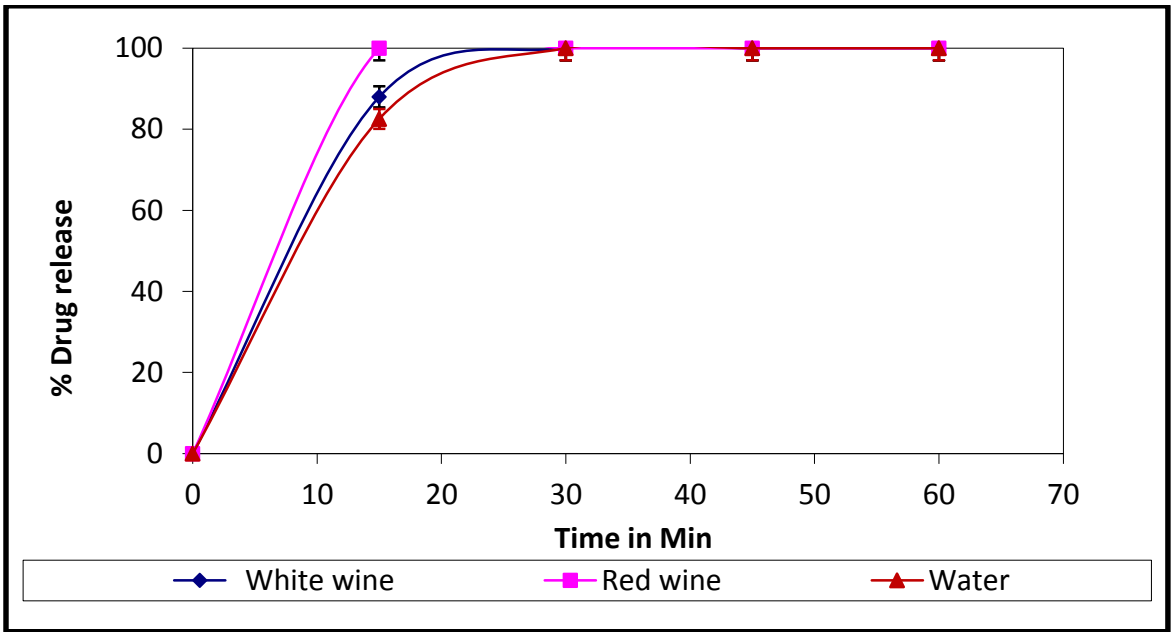

Figure 1: % Drug release of metformin IR in White and Red wine

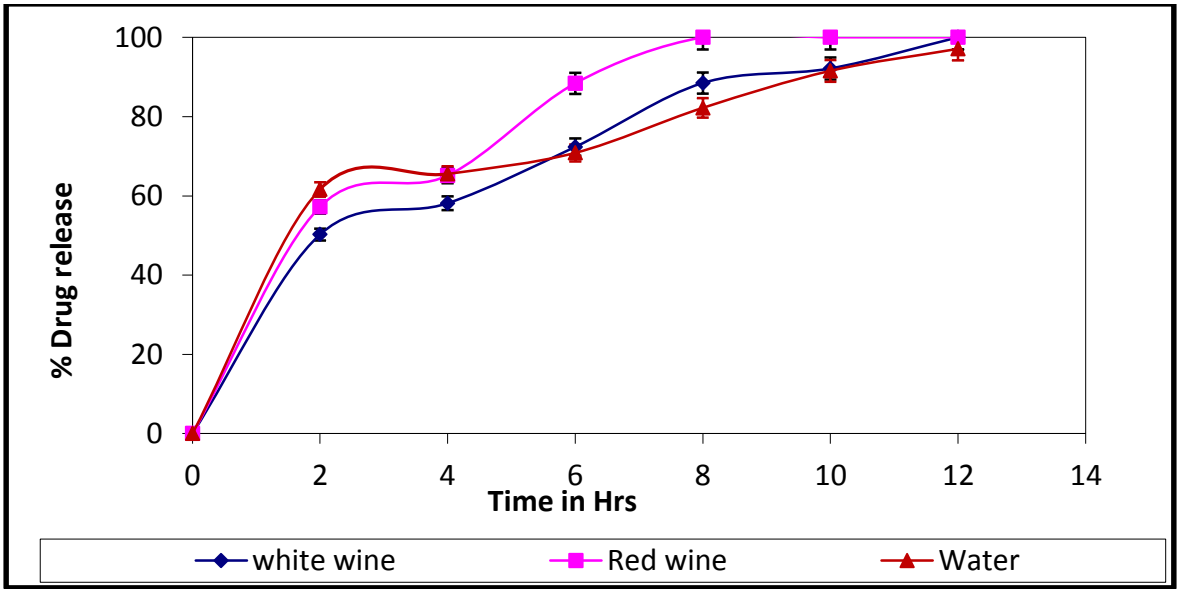

Figure 2: % Drug release of metformin SR in White and Red wine

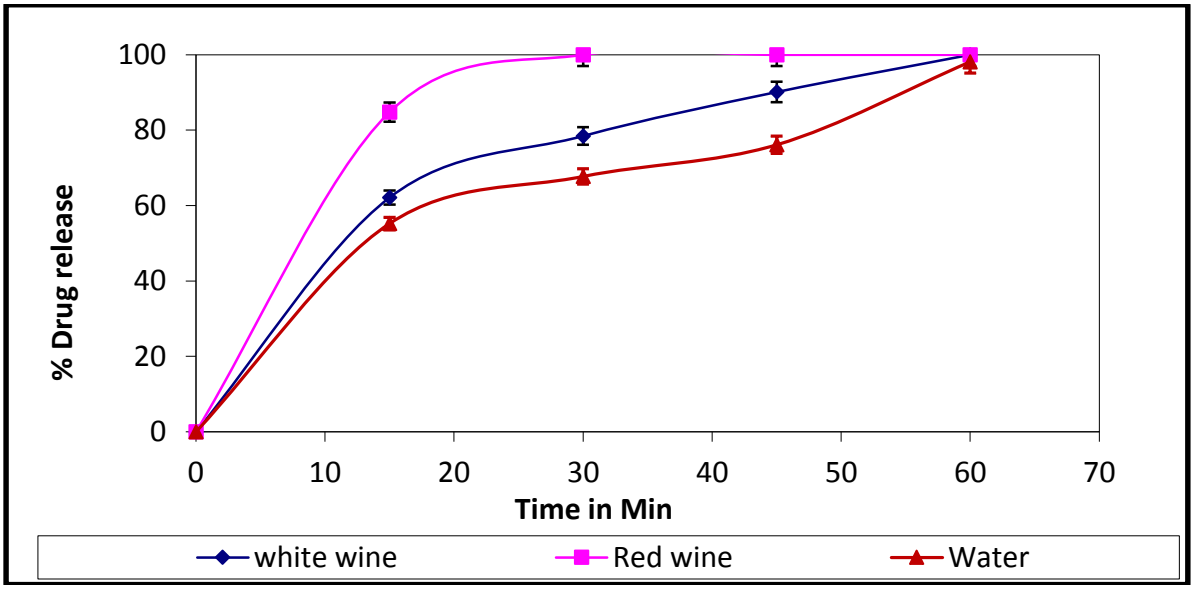

Figure 3:% Drug release of Diclofenac IR in White and Red wine

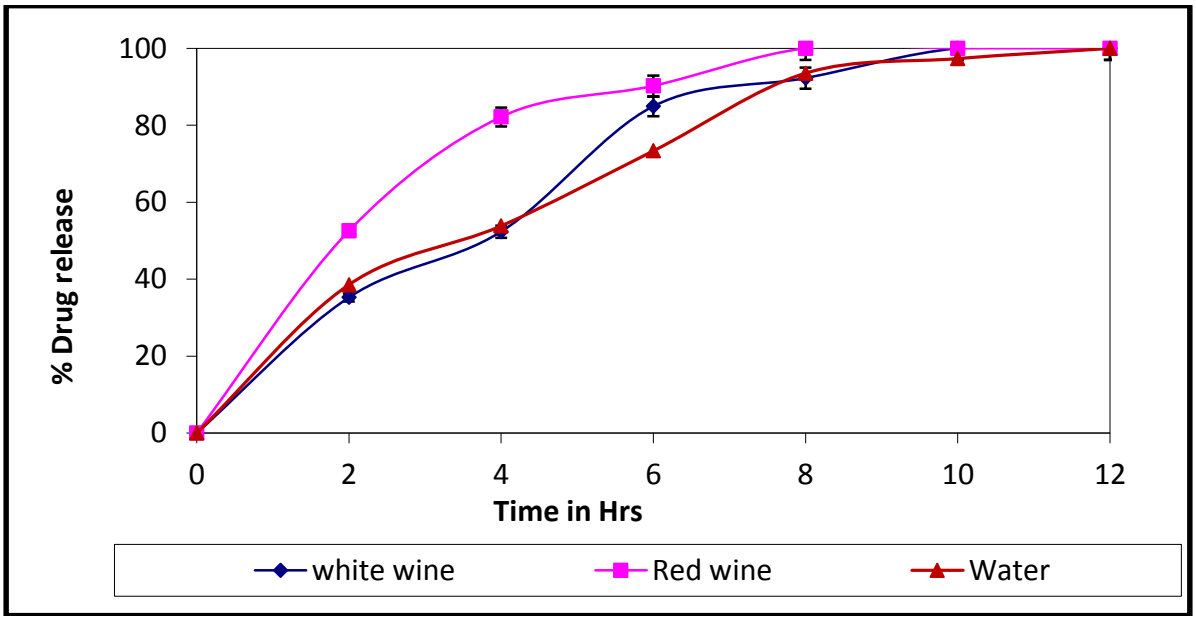

Figure 4: % Drug release of Diclofenac SR in White and Red wine

Table 1: F2 values of dissolution data

Formulations	F2 values	
	Red wine	White wine
Metformin IR	55	79
Metformin SR	48	72
Diclofenac IR	33	53
Diclofenac SR	44	66
Note: IR is instant release and SR is sustained release		

CONCLUSION

The results of present study conclude that, in case of IR formulation, drug release was faster in red wine and white wine as compared to water. Similar results were obtained in case of SR formulations of Metformin and Diclofenac. As alcohol content of red wine is more than that of white wine, the results of present study indicate that the release of drug depended on concentration of alcohol. Thus, the concomitant use of red wine should be avoided during treatment with Metformin and Diclofenac SR formulations to prevent dose dumping effect of alcohol on such SR formulations.

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